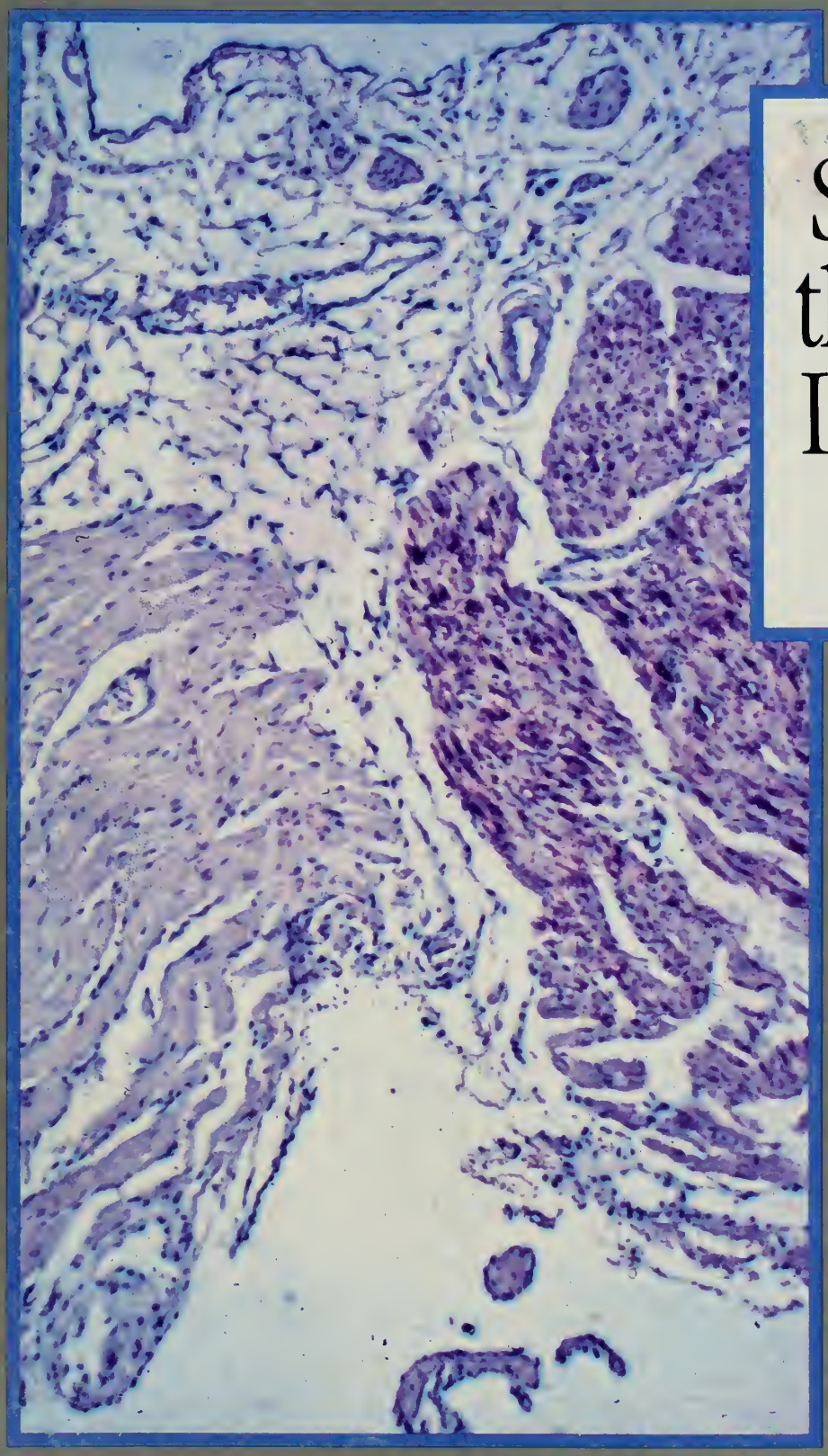
HARVARD MEDICAL

ALUMNI BULLETIN SUMMER 1985



Surveying the Science Landscape at HMS

Eight Investigators

A Woman's Place

Student Directions

Press Relations

Walter B. Cannon

2 Ways To Honor Extraordinary Achievements

■ Put Harvard University on Wedgwood China and you have an heirloom quality collection instantly. Each set cast directly at the Josiah Wedgwood factory in England shows eight different 20th Century views in a lovely mulberry rose pattern on cream.

SHOWN: The Widener Library

Views include — Harvard College Gate, Holden Chapel, Hollis Stoughton, Harvard Houses from the Business School, Straus Library at the School of Business Administration, Memorial Hall and Langdell Hall at the Law School.

Set of Eight, $200

Limited quantities from the 19th Century Collection also available.

■ The Classic Harvard Captain's Chair with the Medical School seal in gold is designed specifically to honor your achievements. Constructed of quality northern hardwood with maple-finish arms and gold trim, it's a faithful reproduction of its 19th Century original and only available through the Harvard Coop.

Also available in all maple $175

HARVARD COOPERATIVE SOCIETY **the Coop**

All available at Harvard Square. Harvard Square store open Mon.-Sat., 9:20 to 5:45, Thurs. till 8:30pm. Call toll free: 1-800-792-5170 within Mass., 1-800-343-5570 outside Mass. for fastest service with your Coop Charge, Mastercard, Visa or American Express.

HARVARD MEDICAL

ALUMNI BULLETIN / SUMMER 1985 / VOL. 59 NO. 2

FEATURES

12 **Profiles in Research:** Eight Investigators from the Preclinical Departments
by Lisa W. Drew

24 **A Lab of One's Own:** Six Faculty Members Ponder the Woman's Place

26 **Making Progress**
by Eleanor Shore

28 **A Day in the Life**
by Orah S. Platt

29 **Changing Male Expectations**
by Judith Herzfeld

30 **Test Tubes and Babies**
by Story C. Landis

32 **Role Modeling for Medical Students . . .**
by Kathryn Beck Kris

33 **. . . And for Graduate Students**
by Joanne S. Ingwall

34 **Meeting the Press:** A Round Table on Science and Journalism

42 **The Making of a Scientist:** Students at the Bench
by Lisa Derman

47 **The Way of Walter B. Cannon:** Remembered by his Daughter
by Marian Cannon Schlesinger

DEPARTMENTS

3 **Pulse**

9 **Student Forum:** Not In My Back Yard
by James Craner

11 **Letters**

52 **Alumni Notes**

60 **In Memoriam:** Alfred Kranes, John Rock, F. Dennette Adams, Stephen E. Hedberg

63 **Death Notices**

Cover: This photograph of the heart's atrioventricular junction, stained with the use of an antibody against atrial natriuretic factor (ANF), reveals the presence of ANF in the atrium but not the ventricle. ANF is a hormone released by the heart that regulates fluid balance in the body (see piece on Jonathan Seidman's work, page 23). Photo by John T. Fallon, associate professor of pathology at Massachusetts General Hospital.

INSIDE H.M.A.B.

The sciences and the humanities are all of a piece," Lewis Thomas '37 said four years ago in a Class Day address, "one and the same kind of work for the human brain, done by launching guesses and finding evidence to back up the guesses." We launched a few guesses of our own in putting together this issue, and found ourselves overwhelmed with a wealth of evidence for each.

Our first guess was that there would be rich material in the story of women in science at HMS. The number of women basic scientists on the faculty, Eleanor Shore found in poring over the records for her piece on the subject, has increased from four to 86 in just the past 16 years—a fact, she writes, that "should surely go down in the annals of HMS as one of its significant accomplishments." Her assessment is followed by the thoughts of four scientists and a psychiatrist on their experiences observing, and taking part in, that accomplishment.

We thought we might find promising things happening in the laboratories of the preclinical departments—and after a first glance we faced only the problem of selection. We also found a distinct trend: genetics is at the heart of at least half of the eight investigations in preclinical laboratories profiled inside—investigations of such varied areas as tumor growth, bacterial virulence, drug-resistant viral mutants, and a hormone released by the heart that regulates fluid balance in the body.

When we looked at the topic of medical students in the lab, we found, in addition to those following M.D./Ph.D. and Health Sciences and Technology tracks, an uncounted subculture doing investigations part-time while taking classes, and others taking summers or whole years off from school to pursue research.

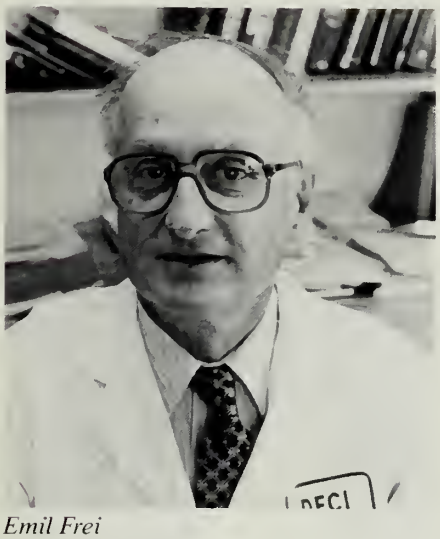
For perspective on the increasingly complex relationship between the scientist and the outside world—via the media—we found a distinguished group of journalists, scientists, and observers with plenty to say on the subject. Last, to include a sense of the scientist outside the laboratory, we turned to Marian Cannon Schlesinger, daughter of physiologist Walter B. Cannon.

In exploring the forces shaping the HMS science landscape, we found a persistent theme that bears mention here. As we contacted scientists in connection with the various articles, through the winter and into the spring, we found them less and less available to write for us and to meet with us. They were becoming increasingly frantic over grant proposals, the majority of which were due in June. Federal budget director David Stockman had found a loophole in the National Institute of Health allocation schedule, and the administration had moved in January to reduce the number of new federal research grants. Although it looked like the changes would not go through, at least not in their most radical form (and they haven't as of this writing), the researchers we were in touch with were painfully aware of the situation.

— Lisa W. Drew

HARVARD MEDICAL
ALUMNI BULLETIN

The *Harvard Medical Alumni Bulletin* is published quarterly at 25 Shattuck Street, Boston, MA 02115 ©by the Harvard Medical School Alumni Association. Third class postage paid at Boston, Massachusetts. Postmaster, send form 3579 to 25 Shattuck Street, Boston, MA 02115. ISSN 0191-7757.



Emil Frei

Emil Frei Named To New Smith Chair

"If you don't believe that cures for cancer can be found, then it is certain you will never find them," says chemotherapy pioneer Emil Frei III. Frei, credited with determining the basic principles of chemotherapy, and with bringing about the first cures of acute lymphocytic leukemia (ALL), has been named the first Richard and Susan Smith Professor at HMS. He is director and physician-in-chief of Dana Farber Cancer Institute, and has been HMS professor of medicine since 1972. The Smiths, whose association with DFCI began 40 years ago, describe their continued support as "a labor of love."

The tradition of Smith giving began with Philip Smith, Richard's father, who in the 1940s founded General Cinema Corporation and was a member of the Variety Club of New England, a philanthropic society of theatre people which sponsored the research of Sidney Farber. With contributions from the Jimmy Fund and the Variety Club, Farber was able to achieve the first clinical remissions of leukemia in children.

Farber went on to found the Children's Cancer Research Foundation (now DFCI), a comprehensive center for cancer research and treatment for children and adults. Philip Smith was a founding trustee of the institution, and continued his affiliation until his death in 1961. When Frei became scientific director in 1973, Richard Smith, already a trustee, became president and chairman of the board of trustees—a position he held until 1980. He is currently vice chairman of the board and chairman of the capital development campaign. His wife, Susan, was a founding member of Friends of the Dana Farber in 1975, and continues to be active in raising money for the institute.

Frei launched his attack on ALL in the 1950s as director of the newly created Cancer Drug Development Program of the National Cancer Institute. At that time, it was commonly believed that cancer could not be cured. "If the door is slammed shut and locked with a dead bolt, which is how most people viewed cancer in those days," says Frei, "there is no hope. But if you have a 'foot in the door,' which there was a scientific basis for believing we had with ALL, you can almost certainly open it."

Within 10 years, the ALL research program created by Frei and his colleague Emil Freireich led to cures. There was a time when patients with leukemia survived an average of two months; today 90 percent of children with ALL are cured. During their collaboration, Frei and Freireich determined the principles that underlie all cancer chemotherapy: treatment with a combination of agents, continued therapy after remission, and prophylaxis of the central nervous system.

"Part of our heritage from Sidney Farber," says Frei, "was his philosophy of clinical cancer research—the resolve to look cancer right in the eye, to study it in the patient." The Frei and Freireich approach was mul-

Emil Frei, Susan Smith, and Richard Smith

PHOTOS BY JUDITH BRENNING

tidisciplinary, including pharmacological research, animal models, and controlled clinical trials. "It is often said that all clinical science is derivative of basic science," Frei comments, "but many profound insights into basic science can come from careful clinical studies." Steps toward finding a cure included using platelet transfusion therapy to stem hemorrhaging caused by ALL-associated platelet depletion; developing a method of quantifying the body's response to therapy, and attaching a meaningful definition to the term "complete remission"; learning how to perform bone marrow aspiration quickly and with least trauma; and examining human cancer cells in culture.

"There is certainly no disagreement about the effectiveness of chemotherapy against some 10 to 12 forms of cancer," Frei points out. "And there's no question but that we still have a long way to go. The real controversy centers on whether the progress we have made against relatively rare cancers can be translated into progress against more common forms. I firmly believe that with some of our newer chemotherapeutic agents and treatment strategies, and others that are coming, improved cure rates for cancers of the head and neck, bladder, cervix, breast, and bone are within our grasp." □

Digestive Diseases Center Formed

An estimated 20 million Americans suffer from digestive disorders such as peptic ulcers, gallstones, and liver diseases, resulting in as many as 200,000 deaths each year. To probe the unanswered questions regarding these diseases and the workings of the digestive tract in general, HMS and Beth Israel and Brigham and Women's hospitals joined forces in September to create the new Harvard Digestive Diseases Center. More than 50 basic scientists and clinicians from the three institutions are involved.

William Silen

The center—one of six funded by five-year grants from the National Institute of Arthritis, Diabetes, and Digestive Diseases—aims to study the structure and function of the entire digestive tract. Supported in its first year by an award of nearly $400,000, it encourages more collaboration on research already under way in the three institutions, and funds "mini sabbaticals" for affiliated investigators who wish to acquire a relevant technique or skill in a laboratory outside the center. It also supports pilot studies by providing start-up funds for young investigators not yet able to compete for other grants, established digestive disease investigators who wish to head in new directions, and scientists just now becoming active in the field.

Physiologist and clinician William Silen, Johnson and Johnson Professor of Surgery and surgeon-in-chief at BIH, is the center's director and principal investigator. In collaboration with the research group of Susumo Ito, James Stillman Professor of Comparative Anatomy, Silen's group studies damage done to the surface epithelial cells of the stomach lining due to irritants such as alcohol, aspirin, and strong salt. Having found that the repair process is much more rapid than was previously recognized, they are now attempting to identify the factors that enhance or inhibit it.

The center's associate principal investigators are Jerry Trier, professor of medicine and head of the Gastrointestinal Section at BWH; Marian Neutra, associate professor of anatomy at HMS; and Raj Goyal, Charlotte and Irving Rabb Professor of Medicine and chief of gastroenterology at BIH.

Currently, Jerry Trier and coworkers—who have spent the past 22 years determining the functional significance of the alimentary tract's structural features—are studying the structure of a highly specialized plasma membrane that forms the microvilli that aid digestion. They plan to use isolated microvillus membrane preparations, together with segments of intact intestine, to investigate changes in the membrane during normal processes such as the absorption of dietary fat. Another project is designed to clarify how microorganisms penetrate the intestinal mucosal barrier.

Marian Neutra's work concerns intestinal epithelium, a single layer of cells that separates the body's interior tissues from foreign substances and microorganisms in the intestine. One type of cell in the epithelium—the goblet cell—secretes large, complex, highly charged glycoproteins that form a gel capable of binding many foreign substances. Using organ and epithelial cell culture with electrical and pharmacologic stimulation, Neutra and colleagues study how the intestinal nervous system controls goblet cells. They also investigate how epithelial cells take up macromolecules and selectively transport them into the bloodstream.

An authority on the esophagus and swallowing mechanisms, Raj Goyal has identified the neural, hormonal, and muscular factors involved in swallowing, transporting food to the stomach, and preventing backup of stomach acid (see Pulse, Spring 1985 *Bulletin*). His work has chiefly involved studies of the lower esophageal sphincter—which opens only during swallowing, so food can enter the stomach—"incompetence" of which can lead to heartburn, ulcers, inflammation of the esophagus, or difficulty swallowing. Goyal and colleagues have discovered that relaxation of the sphincter is controlled by vagus nerves that release a chemical called vasoactive intestinal polypeptide; VIP-containing nerves have since been found to play an important role in neural control of smooth muscle in the GI tract, respiratory system, and blood vessels. The team's

differentiation between two types of muscarinic receptors involved in neurochemical transmission to the sphincter has led to development of new medications for GI disorders. □

Trivial Pursuits: The Medical Edition

"Welcome to the Medical Edition of Trivial Pursuits," an upperclassman greets an entering HMS student in the Class of 1987's second-year show.

"I thought I was in medical school," the student protests.

"Same thing," his classmates assure him in unison.

Preceded by a display of virtuosic gymnastic stunts and interspersed with wacky medical trivia questions, the show reveals a mystical world where cells perform ballet to the *Freeze Fracture Suite*, movie critics Siskel and Ebert review HMS lectures, and Dean Tosteson hosts "Mr. Rogers' Neighborhood." After singing about "My Favorite Things," the dean reveals: "Most of all I like denying someone tenure. Can you say tenure, boys and girls? Of course not. Only *I* can say tenure."

Later on, over at MIT, students in button-down white shirts and black plastic frame glasses repaired with adhesive tape study diligently until all outsiders leave. Then they rip off their "nerd uniforms" and "rock and roll quantitatively" to the tune of "Surfin' USA." "We're not just in med school," they sing, "we're in HST."

Meanwhile, first-year student Bud Weiser (who triple-majored in beer, women, and biochemistry at Wisconsin) finds himself entering the Twilight Zone after having missed Dean Tosteson's lecture. There the skeleton of Walter B. Cannon (who missed the dean's lecture in 1894) tells him he's doomed to hear it for eternity. □

Cavorting cadavers

The "great Lynne Reid"

Allegro Alveoli, *third dance in* Freeze Fracture Suite

Finale

PHOTOS BY JUDITH BRENNING

Knight Duty

This summer, 154 knights-errant will set out from HMS on the next stage of their Quest for the Perfect Career: the Slough of Internship and Residency. They emerged, as usual, victorious from the national Match Day jousting tournament in March. Sixty percent won their first choice program; 86 percent one of their top three choices. Sixty-nine will pursue their quest in Massachusetts, 62 of them in Harvard-affiliated teaching hospitals. The rest will journey across the countryside: 22 to California, 19 to New York, seven to Texas, six to Pennsylvania, and others dotting the landscape singly or in groups of two or three.

As has been the trend over the past five years, fewer are devoting themselves to medicine or sharpening their lances for surgery. More are entering orthopedics, seeking deliverance in OB-GYN, or pursuing the glow of radiology.

The top ten specialty choices:

Medicine	48
Surgery	15
Pediatrics	14
Orthopedics	9
OB-GYN	9
Radiology	9
Primary Care	8
Family Practice	6
Anesthesia	6
Psychiatry	6

Alvin Adell
Cabrini Medical Center, New York City
Preliminary Medicine

Mt. Sinai Hospital, New York City
Anesthesia

David Altobelli
Massachusetts General Hospital
Oral & Maxillofacial Surgery

Edward Andujar
Temple University Medical Center, Philadelphia
Preliminary Surgery (Orthopedics)

Jonathan Asp
Mayo Graduate School of Medicine, Rochester, MN
Orthopedics

Robin Avery
Massachusetts General Hospital
Medicine

Frederic Barker
Massachusetts General Hospital
Neurosurgery

Richard Barth
New England Deaconess Hospital
Surgery

Jeanne Beddoe
Highland Hospital, Rochester, NY
Family Practice

Teresa Benacquista
Long Island Jewish Hospital, New Hyde Park, NY
Surgery

David Benson
St. Mary's Medical Center, Long Beach, CA
Preliminary Medicine (Neurology)

Jeffrey Benson
Montefiore Hospital, The Bronx
Family Practice

Jeffrey Berman
University of Colorado Affiliated Hospitals, Denver
Medicine

David Betteridge
Mt. Auburn Hospital
Preliminary Medicine

Massachusetts General Hospital
Diagnostic Radiology

Bethany Block
Rhode Island Hospital, Providence
Primary Care

Patricia Blood
University of Washington Affiliated Hospitals, Seattle
Preliminary Medicine

Massachusetts General Hospital
Diagnostic Radiology

Claire Bloom
Massachusetts General Hospital
Primary Care

Jay Bonanno
University of California Hospitals, San Francisco
Primary Care

Leslie Boyer-Hassen
Children's Hospital Medical Center
Pediatrics

Scott Bradley
Massachusetts General Hospital
Surgery

Lauren Broussal
Beth Israel Hospital
Medicine

Paulette Bryant
Naval Hospital, Oakland, CA
Pediatrics

Raphael Bueno
Brigham & Women's Hospital
Surgery

Joan Butterton
Massachusetts General Hospital
Medicine

J. Roberto Carreon
University of Washington Affiliated Hospitals, Seattle
Orthopedics

Janet Chaikind
Baylor Affiliated Hospitals, Houston, TX
Pediatrics

Teresa Chan
Brigham & Women's Hospital
Preliminary Medicine

Hospital of the University of Pennsylvania, Philadelphia
Diagnostic Radiology

Duncan Clark
Stanford University Medical Center
Psychiatry

Ellen Clayton
University of Wisconsin Hospitals, Madison
Pediatrics

Lawton Cooper
Highland Hospital, Rochester, NY
Family Practice

Nolan Cordell
VA Medical Center, Long Beach, CA
Medicine

Rosa Crum
Massachusetts General Hospital
Psychiatry

Gary Curhan
Massachusetts General Hospital
Medicine

Jon Davids
University of Colorado Affiliated Hospitals, Denver
Orthopedics

Michaele Delgadillo
Baylor Affiliated Hospitals, Houston, TX
Pediatrics

Sharon Dilley
Cambridge Hospital
Primary Care

Joan Downey
Children's Hospital Medical Center
Pediatrics

Kenneth Dressler
Mt. Sinai Hospital, New York City
Medicine

David Duarte
Martin Luther King Jr./Drew,
Los Angeles
Surgery

Ann Duerr
Children's Hospital Medical Center
Pediatrics

Cheryl Dunnett
University of California Affiliated
Hospitals, Irvine
Medicine

Amy Ehrlich
Beth Israel Hospital
Preliminary Medicine

Tufts-New England Medical Center
Physical Medicine and Rehabilitation

Jeffrey Fenwick
Washington University School of
Medicine, St. Louis, MO
Otolaryngology

William Fletcher
Mayo Graduate School of Medicine,
Rochester, MN
Medicine

Eduardo Flores
University of Texas SW Affiliated
Hospitals, Dallas
Medicine

Eugene Foley
New England Deaconess Hospital
Surgery

Neil Freedman
Beth Israel Hospital
Medicine

Sharon Freedman
Beth Israel Hospital
Preliminary Medicine

Massachusetts Eye & Ear Infirmary
Ophthalmology

Nancy Gagliano
Brigham & Women's Hospital
Medicine

Clifford Gall
Brigham & Women's Hospital
Neurosurgery

Cheryl Goffney
Baylor Affiliated Hospitals, Houston, TX
OB-GYN

David Green
UCLA Medical Center
Otolaryngology

SueJane Grosso
Waterbury Hospital, Waterbury, CT
Preliminary Medicine

NYU Medical Center
Diagnostic Radiology

Geeta Gupta
University of California Affiliated
Hospitals, Irvine
Medicine

James Guyton
University of Iowa Hospitals, Iowa City
Orthopedics

Priscilla Harrell
Cambridge Hospital
Transitional

Agiua Heath
Highland General Hospital, Oakland, CA
Medicine

Stanley Hemsley
St. Christopher's Hospital, Philadelphia
Pediatrics

Cristela Hernandez
University of Texas SW Affiliated
Hospitals, Dallas
OB-GYN

Astrid Holberg
Harbor UCLA Medical Center,
Torrance, CA
Pediatrics

Frank Howard
Brigham & Women's Hospital
Medicine

Mark Howard
Harbor UCLA Medical Center,
Torrance, CA
Orthopedics

Paul Huang
Massachusetts General Hospital
Medicine

Marlon Hughes
University of Washington Affiliated
Hospitals, Seattle
Diagnostic Radiology

Helen Hunt
Massachusetts General Hospital
Primary Care

Yuri Imanishi
Rhode Island Hospital, Providence
Primary Care

Silvio Inzucchi
Yale-New Haven Medical Center
Medicine

Bengt Ivarsson
Yale-New Haven Medical Center
Surgery

Pamela Jackson
Children's Hospital Medical Center
Pediatrics

Lynt Johnson
Massachusetts General Hospital
Surgery

Paula Johnson
Brigham & Women's Hospital
Medicine

Sandra Jones
Baylor Affiliated Hospitals, Houston, TX
Otolaryngology

John Jordan
Mt. Auburn Hospital
Preliminary Medicine

University of California Hospitals,
San Francisco
Diagnostic Radiology

David Joseph
Salem Hospital, Salem, MA
Preliminary Medicine

Massachusetts General Hospital
Anesthesia

Richard Kaplan
Children's Hospital, Philadelphia
Pediatrics

Elizabeth Kaufman
Presbyterian Hospital, New York City
Medicine

Richard Kenney
Duke University Medical Center
Medicine

Eugenie Komives
Beth Israel Hospital
Preliminary Medicine (OB-GYN)

Michael Koren
The New York Hospital
Medicine

Rhonda Kost
Yale-New Haven Medical Center
Medicine

Harlan Krumholz
University of California Hospitals,
San Francisco
Medicine

David Kusner
Case Western Reserve University
Hospital, Cleveland
Medicine

Mitchell Laks
research

Albert Einstein College of Medicine
Diagnostic Radiology

Michael Landzberg
Columbia-Presbyterian, New York City
Medicine

Philip Lane
University of California Hospitals,
San Francisco
Pathology

Dana Leifer
Massachusetts General Hospital
Neurology

Simon Lejeune
Massachusetts General Hospital
Preliminary Pediatrics

Cambridge Hospital
Psychiatry

Chris Liacouras
Children's Hospital, Philadelphia
Pediatrics

Karen Lind
McLean Hospital
Psychiatry

Jeff Lindsay
University of Texas SW Affiliated Hospitals, Dallas
Preliminary Surgery (Orthopedics)

Kwok Ming Lo
Brigham & Women's Hospital
Medicine

Susan Lobel
Brigham & Women's Hospital
OB-GYN

Evan Loh
Brigham & Women's Hospital
Medicine

Frederick Long
Beth Israel Medical Center, New York City
Preliminary Surgery

Stanford University Medical Center
Anesthesia

Joan Mannick
Brigham & Women's Hospital
Medicine

Martin Martin
Harbor-UCLA Medical Center, Torrance, CA
Pediatrics

Jeffrey Matthews
Beth Israel Hospital
Surgery

Jeffrey Miller
Cambridge Hospital
Transitional

Massachusetts General Hospital
Anesthesia

Joan Miller
Newton-Wellesley Hospital
Preliminary Medicine

Massachusetts Eye & Ear Infirmary
Ophthalmology

L. Kendrick Mills
Brigham & Women's Hospital
Medicine

Lewis Milrod
Beth Israel Hospital
Preliminary Medicine

Brigham & Women's Hospital
Neurology

Steven Mirabello
Santa Barbara Cottage Hospital, Santa Barbara, CA
Preliminary Surgery

Hospital for Joint Diseases, New York City
Orthopedics

Constance Monitto
Children's Hospital Medical Center
Pediatrics

Roger Montgomery
Boston City Hospital
Medicine

Alvin Morales
Lemuel Shattuck Hospital, Jamaica Plain, MA
Transitional

Massachusetts General Hospital
Anesthesia

Edward Murphy
St. Clare's Hospital, Schenectady, NY
Family Practice

Michael Myers
Mt. Auburn Hospital
Primary Care

Sarah Neilly
Beth Israel Hospital
Medicine

Jed Nuchtern
University of Washington Affiliated Hospitals, Seattle
Surgery

Dale Oates
New England Deaconess Hospital
Preliminary Medicine

Massachusetts Eye & Ear Infirmary
Ophthalmology

Richard O'Brien
Massachusetts General Hospital
Medicine

Regis O'Keefe
New England Deaconess Hospital
Preliminary Surgery

University of Rochester, Rochester, NY
Orthopedics

Dennis Orgill
Brigham & Women's Hospital
Surgery

Fred Orlando
Newton-Wellesley Hospital
Preliminary Medicine

Lenox Hill Hospital, New York City
Ophthalmology

Adrian Ortega
Massachusetts Eye & Ear Infirmary
Research

Orlando Ortiz
Nassau Hospital, Mineola, NY
Preliminary Medicine

Long Island Jewish Hospital, New Hyde Park, NY
Radiology

Patricia O'Shea
Boston VA Medical Center
Medicine

Elizabeth Petri
Massachusetts General Hospital
Medicine

Earl Potts
Montefiore Hospital, The Bronx
Medicine

Richard Renslo
Newton-Wellesley Hospital
Preliminary Medicine

Harbor-UCLA Medical Center, Torrance, CA
Diagnostic Radiology

Drucilla Roberts
Brigham & Women's Hospital
OB-GYN

Gregory Robertson
University of Arizona Affiliated Hospitals, Tucson
Surgery

Daniel Rosa
Lenox Hill Hospital, New York City
Medicine

Jill Rosenthal
Massachusetts General Hospital
Preliminary Medicine (Dermatology)

Robert Sackstein
Jackson Memorial Hospital, Miami, FL
Medicine

Judith Salerno
Georgetown University Hospital, Washington, DC
Medicine

Suketu Sanghvi
St. Francis Hospital, Hartford, CT
Preliminary Surgery

Massachusetts General Hospital
Orthopedics

Robert Schulte
New England Deaconess Hospital
Preliminary Surgery

Tufts-New England Medical Center
Orthopedics

Joyce Show
Tufts-New England Medical Center
Medicine

Baptiste Shunatona
University of Oklahoma Tulsa Medical College
Family Practice

Jonathon Sillman
St. Joseph Mercy Hospital, Ann Arbor, MI
Preliminary Surgery

University of Michigan Hospitals, Ann Arbor
Otolaryngology

Scott Smythe
St. John Hospital, Detroit
Transitional

Massachusetts General Hospital
Anesthesia

Sheryl Spitzer-Reznick
University of Wisconsin Affiliated Hospitals, Madison
Family Practice

Linda Starace
NYU Medical Center
OB-GYN

John Steichen
Massachusetts General Hospital
Neurosurgery

Elizabeth Stewart
University Health Center, Pittsburgh
OB-GYN

Regina Stuart
New England Deaconess Hospital
Surgery

Scott Swanson
Brigham & Women's Hospital
Surgery

Geoffrey Tabin
University of Colorado Affiliated Hospitals, Denver
Preliminary Surgery (Orthopedics)

Loyal Tillotson
Duke University Medical Center
Medicine

William Torrey
Dartmouth-Hitchcock Center,
Hanover, NH
Psychiatry

So-Fai Tsang
University of Washington Affiliated
Hospitals, Seattle
Medicine

Sharee Umpierre
University Hospital, San Juan, PR
OB-GYN

Robert Van Wesep
University of Maryland Hospital,
Baltimore
Pathology

Mark Vierra
Stanford University Hospital
Surgery

Michael Weiss
Brigham & Women's Hospital
Medicine

Melissa Welch
University of California Hospitals,
San Francisco
Primary Care

Kathleen Welsh
University of California Hospitals,
San Francisco
Medicine

Janey Wiggs
Beth Israel Hospital
Medicine

Stephen Wintermeyer
Walter Reed Medical Center,
Washington, DC
Medicine

Barbara Woo
Brigham & Women's Hospital
Medicine

Rebecca Wurtz
Rush-Presbyterian-St. Luke's
Medical Center, Chicago
Medicine

Elena Yanushpolsky
Brigham & Women's Hospital
OB-GYN

Jennifer Yolles
Beth Israel Hospital
Preliminary Medicine

McLean Hospital
Psychiatry

Stephen Zucker
Brigham & Women's Hospital
Medicine

Susan Zweizig
LAC-USC Medical Center, Los Angeles
OB-GYN □

STUDENT FORUM

Not in My Back Yard

by James Craner '88

When I told my friends I would be coming to Boston to attend Harvard Medical School, they were pleasantly surprised. A great education, a fun city . . . and besides, Massachusetts has a beverage container deposit law. "With *that*, you'll definitely be happy," they told me. That's not the typical response to such news, but then, my interest in medical school was due in part to my environmental activism—including two years I spent lobbying and organizing citizens in support of a deposit law in New Jersey. Yes, I mean the five-cent refund you receive when you return your soda and beer containers to the store.

In the fall of my junior year in college, I had testified before the New Jersey Senate Energy and Environment Committee about the need for the proposed Worker and Community Right to Know Act—which would require industries and businesses to label hazardous chemicals in the workplace and to train employees how to handle them properly. This law would also allow community residents and firefighters to learn the names and health hazards of chemicals used, stored, manufactured, or emitted by companies throughout the state.

On one side of the Senate hearing room were several hundred union workers, firefighters, and community activists; on the other side were a multitude of highly paid lobbyists representing the New Jersey Chamber of Commerce, the Chemical Industrial Council (which represents the 70 largest chemical and petrochemical companies in the state), and pharmaceutical and plastics companies. Each lobbyist testified that "anti-business" regulatory "nightmares" like the Right to Know would drive these industries—which employ over 130,000 people—out of state. No number of compelling accounts of workers contracting cancer or children playing on abandoned dumpsites could dissuade them.

After a two-year battle, the Right to Know bill was finally signed into law. Going through that process shaped my ambitions. I learned to compromise and delegate responsibility, and to accept many inevitable frustrations. Though tangible results did not come often or easily, I saw that my contribution was significant. This insight gave me the patience to do the "scut work" necessary for effective political organizing. These self-realizations were the criteria I used to judge whether medicine would be an appropriate career choice.

My interest in environmental issues began during high school, when I ran the glass and newspaper recycling program for my hometown of Springfield, New Jersey—a quiet, residential suburb only a short drive from the infamous turnpike lined with smokestacks, refineries, and huge garbage landfills. I continued to organize recycling efforts at Princeton University; by the middle of my sophomore year, I had also transformed a dormant student organization, Princeton Environmental Action, from a project-oriented group to one devoted to political action. PEA activities developed my political awareness and gave a direction to my education; I decided to major in chemistry, a field I could apply directly to the issues that concerned me.

Later that year, at a conference for New Jersey college environmental leaders, I met Madelline Hoffman, leader of a local citizens' environmental organization in Newark's Ironbound neighborhood. The Ironbound is a working-class neighborhood with large Portuguese, black, and white ethnic populations; the residential area is mixed with heavy manufacturing industries, warehouses, and nearby refineries. I was shocked by Hoffman's pictures of chemicals being dumped down sewers late at night at

a "reprocessing" facility, fires at abandoned warehouses where thousands of drums of chemical wastes were illegally stored, and tanker trucks carrying hazardous chemicals from local warehouses through neighborhood streets. I learned that one waste-handling company, SCA Services, which was reputed to be a "midnight dumper" with ties to organized crime, was planning to expand its facility right in the neighborhood.

These were not academic problems. At stake were the air people breathed and the water they drank. Even today, the At-Sea Incineration Company is seeking to build a 7.5 million gallon toxic waste "tank farm" and marine terminal. Chemical wastes from all over the East Coast would be loaded on an incinerator ship and then burned 100 miles off the New Jersey coast. Residents from Newark, Jersey City, and the entire Newark Bay area, deeply concerned that hundreds of trucks loaded with chemical wastes will drive through residential streets, have coalesced to fight the proposal.

Through my initial contacts at that conference I later met Jim Lanard, lobbyist for the New Jersey Environmental Lobby (and the *only* professional environmental lobbyist in the state). Jim asked me to attend a statewide organizational meeting of residents, firefighters, labor union health and safety representatives, and environmentalists to draft the Worker and Community Right to Know law.

I was astonished to learn of the incredible number of illnesses caused by occupational exposures to hazardous chemicals—in both traditional chemical manufacturing jobs and smaller businesses such as dry cleaning—many of which a Right to Know law could prevent. Most notable is the 1980 Chemical Control inferno, when over 50,000 drums of unmarked chemical wastes exploded, sending fumes of unknown chemicals for days into the metropolitan New York-New Jersey area. Many firefighters suffered chemical burns and lung injuries from breathing fumes from barrels of unlabeled chemicals; the long-term health effects are as yet unknown.

Another example is the Johns Manville Company, where for years thousands of workers had been exposed to high levels of asbestos dust even after company officials knew of the dangers. Ten to 30 years later, many of these workers have contracted lung cancer, including mesothelioma, a rare form associated specifically with asbestos exposure.

My first tasks for the Right to Know movement were to interest and educate other Princeton students about the issue and to organize letter-writing campaigns to state senators who were reviewing the bill in committee. I soon found myself writing articles, doing research, and visiting my local state senator. I attended coalition meetings in New Brunswick every other week, contributing and critiquing portions of substantive text to the bill, then moved on to organize labor leaders and citizens in my legislative district, which comprised most of Mercer county, including Princeton and Trenton.

During the two years we fought for passage of the Right to Know bill, PEA members became actively involved in national wildlife and energy conservation, reauthorization of the federal Clean Air and Clean Water acts, and, on the state level, passage of a beverage container deposit law—the "bottle bill"—and a law to require water companies to test for organic pollutants in public water supplies. I continued to meet people in government, industry, and research, as well as citizens involved in these issues—among them Lois Gibbs, leader of the Love Canal Homeowners Association, who spoke at Princeton.

Two statewide organizations, the New Jersey Environmental Lobby and the Youth Environmental Society, asked me to serve on their boards, to work on fund raising and public relations in addition to contributing to decisions that affected environmental policy and education. In my senior year I also organized the first student political action committee in New Jersey, PEAPAC. PEAPAC raised over $1,000, which we used to print literature and run radio advertisements for state Senate candidates we had endorsed—including our local senator, Jerry Stockman, who had played an important role in moving the Right to Know bill through his committee.

Waste disposal—both industrial chemicals and municipal garbage—became my main interest. I learned of the need to establish new facilities, such as incinerators and recycling plants, to replace landfills which now contribute to air and groundwater contamination. In a small, densely populated state like New Jersey, finding a site for such a facility is extremely difficult. Though everyone benefits from having a safe alternative to leaking landfills (or worse, to wanton, illegal disposal of toxic wastes in open fields or abandoned warehouses), no community wants to host a new facility and risk the potential health hazards. Because of this NIMBY syndrome—"Not In My Back Yard"—no state has constructed a new hazardous waste facility in the past 10 years; indeed, in the entire nation only a few remaining landfills and incinerators, built before environmental standards were established, continue to accept hazardous waste for disposal.

When I applied to medical schools, my parents, college premed adviser, and interviewers all asked how I knew medicine was the right choice for me. I replied that I saw a great need for health professionals with strong scientific and political backgrounds who can use their skills and authority to help other concerned citizens prevent or minimize pollution hazards. Every environmental and public health problem in which I had been involved could have been prevented to a large degree if people with the proper expertise had influenced political decisions directly relevant to public health policy. The Right to Know movement is a prime example. Though a few medical and public health officers' associations endorsed the bill, they did not reach out to educate and inform citizens of the importance of such a law. Such an effort would have provided a big boost to the arguments of ordinary citizens and environmentalists before the state legislature.

Physicians can have a strong impact on pollution problems precisely because they possess the skills to deal with scientific issues, call in resources to evaluate problems, and gain the confidence of the community. Doctors should inform themselves about the hazards of chemical exposure, become familiar with local industries and dumpsites, and establish contact with the local public health officer or municipal engineer. They can help assess the potential health impacts of a proposed incinerator, negotiate with local companies for reasonable pollution controls and public accountability, or help local or state officials set emission standards for industries. By assessing medical risks, physicians can also play a key role in establishing the necessary safeguards for monitoring hazardous waste facilities to ensure that they comply with safety standards and remain accountable to the community.

Today it is not enough for doctors to treat patients whose water supply has already been contaminated or who have already been exposed to hazardous chemicals in the workplace. The cancers associated with exposure to many chemicals—in the workplace, drinking water, the air; from pesticides on lawns and foods, solvents, dyes, paints, seepage from landfills miles away—take many years to proliferate, often long after the source has been discarded or forgotten. More than ever before, "healing" can be best accomplished through prevention.

A group of physicians at the University of Medicine and Dentistry of New Jersey—the Task Force on Solid Wastes—recently published a report urging the governor and legislature to adopt policies, such as tax breaks and penalties, to reduce the amounts of hazardous wastes generated in New Jersey, and to promote full-scale recycling of municipal garbage and adopt strict air emission standards for new garbage incinerators to protect the public and the environment. I hope this report will be followed up with continued action by more members of the medical community.

Though I am not sure now what area of medicine I will enter, I know I will want to participate in local environmental issues, combining my political acumen, medical knowledge, and organizational skills. I hope others concerned about the environment will consider entering medicine, and that more premed students will become politically educated and involved. I also hope my fellow medical students will think more from a preventive view, and, of course, I would like to see established doctors become more active in environmental issues.

When I travel home to New Jersey, I will always have those huge landfills and smokestacks to welcome me. That tainted reminder is a call to action that we, as physicians, must answer. □

LETTERS

Countway Legacy

Reading the fascinating account of the Countway legacy in the Spring 1985 *Bulletin* stirred some memories.

Through the 1950s, while I was working with Dr. Denny-Brown at Boston City Hospital, I did some consulting work to allow my family to eat and, in turn, allow me to remain in the restless backwater of academic medicine. In 1953 or '54 (I regret I cannot lay my hand on the consultation note) I was called to Longwood Towers by a Brookline practitioner who was caring for Mr. Countway. Countway was very disabled and quite helpless, attended by nurses under the direction of his very concerned sister. I believe I was called to see him because he had the difficult symptom of bruxism, compared to which the screech of new chalk on a blackboard sounds like Galway playing flute. Pharmacological treatment for movement disorders was not far advanced at that point, but my HMS education allowed me to find the appropriate chemicals, mix them properly, make the patient and his attendants more comfortable—and, I like to think, give HMS a library.

It would be of great interest to know about Mr. Countway's origins. Was he from Chelsea? What high school had he gone to? What was his family's background?

—Joseph M. Foley '41

Editor's note: According to research by Robert W. Lovett of Harvard Business School's Baker Library, Francis Countway's father, David L., was from Halifax, Nova Scotia, and his mother, Ada M. (Reid), was from Rockland, Maine. The close-knit family lived in Somerville from 1879 until the father's death in 1911. He had been an insurance agent and salesman. Francis Countway dropped out of Somerville High School at age 16 in 1892.

The interesting article on Countway Library was my first read in the new issue. Good work—but Vanderbilt Hall long antedates 1956. And was it Hugh Stubbins himself who designed the library? I have heard it was a now-deceased associate. Was it the model for the prize-winning design at Exeter by a different firm?

—M.C. Webb

Editor's note: Construction of Vanderbilt Hall was started in 1926, and was completed the following year. According to Merle Westlake of Stubbins Associates, Countway Library was designed by Hugh Stubbins and Peter Woytuk. It was not a model for the Exeter library, but many architects have studied HMS's program for designing the library, and incorporated some of the same solutions.

The article on Countway Library describes some of Francis Countway's innovations in promoting Lever Brothers' products, including Lux soap. I'd like to add a note. The person responsible for the great success of the Lux radio programs in the early 1940s was Daniel J. Danker Jr. of Brookline, my brother-in-law. After attending Country Day School, Exeter, and Harvard College (Class of 1925), Daniel was picked from the 12 Harvard College graduates interviewed that year by J. Walter Thompson advertising agency. He rose rapidly in the company, becoming executive vice president of the Los Angeles office. Daniel died suddenly of an acute heart attack in 1944. His daughter, Susan, lives in California. His sister Mary Danker (Radcliffe 1925) married me in 1931. She died in January 1983.

—John Adams Jr. '29

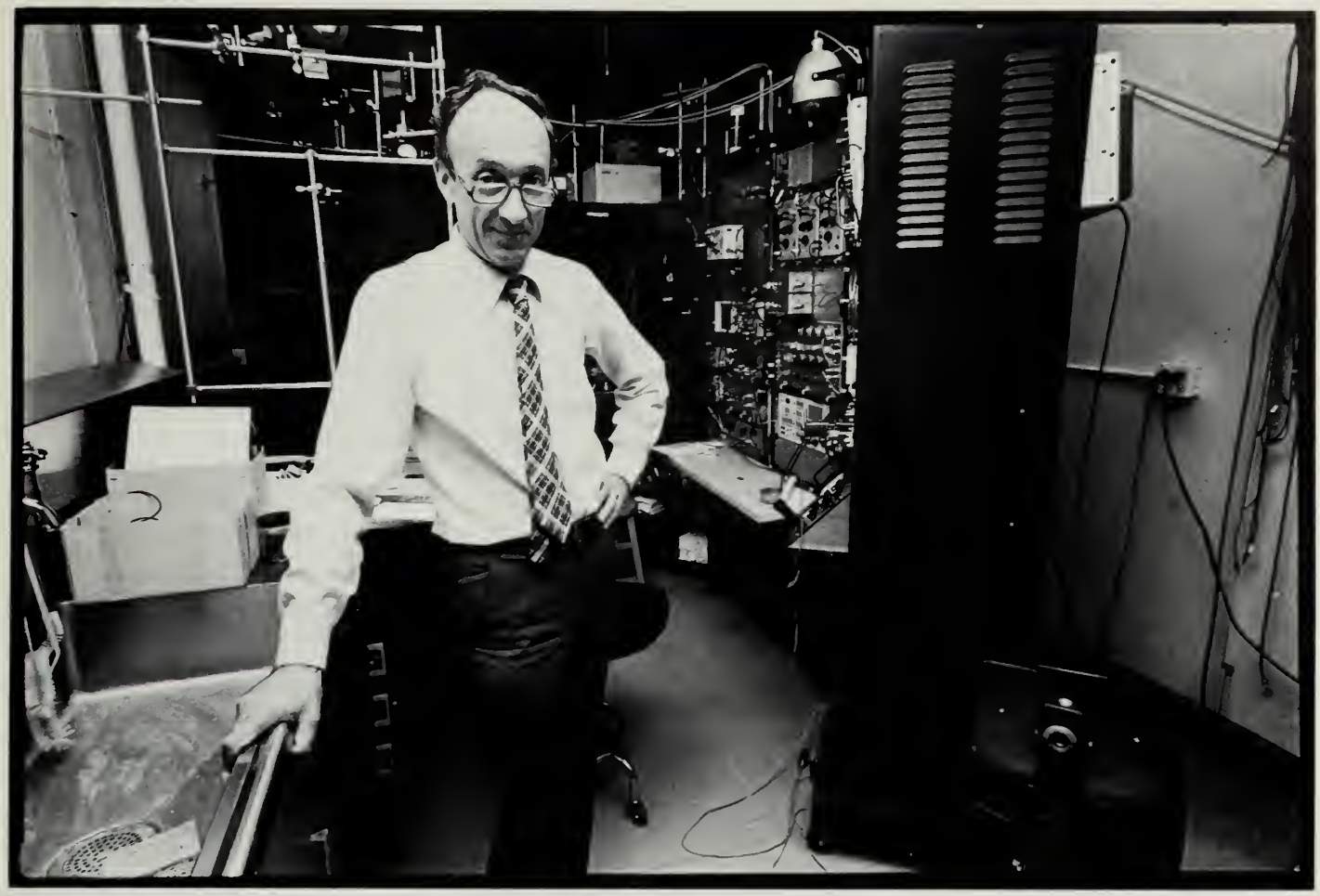
Eight Investigators
from the
Preclinical Departments

Profiles in RESEARCH

by Lisa W. Drew

After we had made the decision to take a look at the work of a handful of Harvard Medical School's basic scientists, we faced the impossible task of selection. Of the 2,408 members of the Faculty of Medicine, 208 are in the preclinical departments. So we consulted the heads of eight departments—Baruj Benacerraf (Pathology), Bernard Fields (Microbiology and Molecular Genetics), Irving Goldberg (Pharmacology), Howard Green (Physiology and Biophysics), Elizabeth Hay (Anatomy and Cellular Biology), Philip Leder (Genetics), David Potter (Neurobiology), and Charles Richardson (Biological Chemistry)—and asked each for the name of one faculty member whose work may have clinical implications.

The result is a list of scientists whose titles range from assistant professor to named professorship—and whose work may one day yield results ranging from long-term vaccines against virulent bacterial disease, to control over the heart's own pressure-regulatory mechanism, to treatments for myopia.



Elio Raviola

"You can get eye elongation, or nearsightedness, by modifying the visual input, which tells you that the nervous system is involved."

Some 10 years ago, professor of human anatomy Elio Raviola was conducting sophisticated studies of photoreceptor cells in the retina when he found himself also embarking on a simple, "19th-century physiology" investigation of nearsightedness in the monkey. Over the past decade his work on the retina has evolved into an elegant mapping of its mechanisms with colleague Ray Dacheux—and his monkey experiments, in collaboration with neurobiologist Torsten Wiesel, have yielded the first animal model of myopia and clues to its causes.

The myopia work started as an incidental finding of Wiesel's studies with David Hubel on the visual cortex. They had been suturing shut the eyelids of newborn monkeys to study the effects of visual deprivation on the cortex, and had been surprised to find myopia in the closed eyes. Wiesel took a short walk downstairs in Building B to share the finding with Raviola. The two agreed "that it could be an interesting line to develop, since very little is known of the mechanism of refractive errors," recalls Raviola. "Ideally, if one knows the mechanism, one can develop preventive measures. You have to realize: 25 percent of the American population has myopia, and in Orientals the figures are much higher."

The myopic eye is usually longer than an eye with normal vision. Scientists have long wondered whether the elongation is due to genetic factors, or whether it is determined by excessive near work. Raviola and Wiesel (now at Rockefeller University) have established with a number of experiments that "you can get eye elongation by modifying the visual input, which tells you that the nervous system is involved."

Their "first striking result" came when they raised monkeys with sutured lids in the dark (the eye can discern some light and shadows through a closed lid), and found that myopia did not develop. The eye did become

PHOTOS BY JERRY BERNDT

longer, however, when the cornea was made opaque without suturing the lids.

In the literature they found many previously unrelated observations that now made sense. Children with opacities in the cornea or vitreous body, for example, develop myopia in that eye—as do children with a drooping upper lid. In every case the eye is elongated—and the disturbance has always been in the perinatal period. "Basically," Raviola says, "we have human equivalents of our lid suturing."

They next looked for clues to the role of the nervous system. They paralyzed accommodation, or the ability to focus on nearby objects, by instilling atropine into the eye—a technique that has been tried with mixed results in human children who have had signs of developing myopia. "We did this on two species of monkeys," explains Raviola. "It turned out that if you paralyze accommodation in the stumptail macaque, myopia doesn't develop. Surprisingly, in the rhesus macaque the eye still gets myopic—with atropine or when you cut the optic nerve.

"So now we are beginning to think there are many ways the growth of the eye is regulated by the nervous system. Accommodation is one; another possibility is that there is a local mechanism: perhaps the retina releases molecules that regulate eye growth. It might turn out that the mechanisms vary from individual to individual."

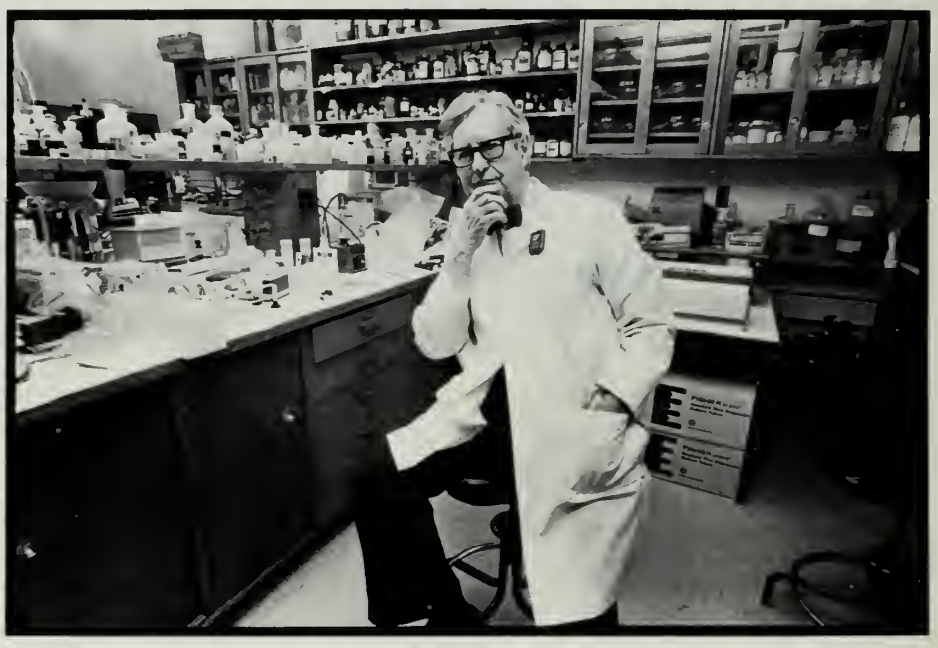
Raviola says that "it is no longer so much fun working on this project since Torsten went to Rockefeller. I miss our lunches at the Legal Sea Food on our way back from the Primate Center in Southborough, eating chowder and talking of our experiments."

With colleague Ray Dacheux, Raviola has been studying how the mammalian retina processes visual information. When the two started collaborating five years ago, according to Raviola, they "began to combine physiology and structural techniques to solve the issue of how retinal neurons interact to generate the message that the ganglion cells deliver to the brain."

Raviola is interested in the retina as "a portion of the nervous system which has moved to the periphery. In a sense the posterior eye cup is an ideal tool, an intact piece of nervous system that you maintain *in vitro*. You can control the input, or photons, with absolute precision. The output, or the message the retina sends to the brain, is relatively well known. The point is to find out what kind of processing occurs within the retina between the photoreceptors and the ganglion cells."

To do that, Raviola and Dacheux record with microelectrodes the responses of the various retinal neurons to light. Then they stain the cell from which the recordings have been obtained, and use the electron microscope to study how "cells talk to one another through synapses—from the photoreceptors to the ganglion cells."

So far, working on the rod system, which the eye uses in dim light, they have identified the responses and studied the connections of three of the neurons inserted in series along this pathway (a horizontal, a bipolar, and an amacrine cell). They are working now on the ganglion cells, which form the last neuron in the retina that processes rod signals and transfers them to the brain. When they have finished, they will "for the first time have a complete neural channel through the retina, and will know the mechanism by which this portion of the nervous system processes dim light signals."



Manfred Karnovsky

Manfred Karnovsky's recent investigations into the biochemistry of the "sleep factor"—a substance he and two colleagues isolated three years ago—have led him to "a rather daring thought." He and others have found links among functions of the nervous system, slow-wave sleep, and cellular immunity. "For a long time there's been a field of neuro-endocrinology," he says. "Now there seems to be developing a field I like to call psycho-neuro-immuno-biology—although I don't know which comes first."

It took the research team of Man-

fred Karnovsky, John Pappenheimer, and James Krueger 15 years of painstaking work to isolate and identify Factor S, a substance that causes sleep in mammals, across species, in minute quantities. In collaboration with a commercial laboratory, the investigators finally purified enough Factor S for complete analysis: from over five tons of human urine, they derived 30 micrograms, or less than a grain of salt. The new micro-process known as fast-atom-bombardment mass spectrometry, done with the help of Martin and Biemann at MIT, revealed Factor S to be a muramyl peptide, probably derived from the cell walls of bacteria in the intestine.

Since that finding, Pappenheimer has been working on the absorption of muramyl peptides and aspects of the effects of oxygen tension on slow-wave sleep, Krueger has continued studies on sleep-inducing properties of a number of biologically related substances, and Karnovsky has "spent a lot of time showing to my own satisfaction that you *do* find these substances not only in the liver and the kidney, but also in the brain."

Karnovsky hypothesizes that mammals regulate the effect of the vitamin-like muramyl peptides. "Why don't we sleep all the time?" he asks. "We believe that in the brain there are two enzymes under some circadian rhythm control, one that amidates, and another that deamidates, muramyl peptides. We showed the former to activate and the latter to inactivate the sleep-inducing qualities of those compounds. In other words, we're looking for the mechanism that allows these things to be stored, and then turned on."

Most recently, Karnovsky has been looking at the well-established phenomenon of how muramyl peptides activate macrophages, or white blood cells—a natural question for his lab. For over 25 years he has been interested, independent of sleep research, in establishing how white blood cells phagocytize, or ingest and kill bacteria—and therefore has "all sorts of macrophage-suitable techniques and enzyme studies at my fingertips." Through all his work runs a basic involvement with cell membranes.

Using radioactive markers, Karnovsky and his students have found specific binding sites on white cells that recognize muramyl peptides, which then activate the cell. Following up on a hypothesis of two theoretical biologists at the Salk Institute, he has also found that seratonin (a nerve transmitter substance implicated in sleep promotion) shares binding sites—and the ability to activate the macrophage—with muramyl peptides.

"So now we have a neurotransmitter that activates a part of the cellular immune system," Karnovsky says. "The circle is closing—that is, slow-wave sleep, cellular immunity, and the nervous system generally have some common aspects."

Others have shown that macrophages treated with muramyl peptides release interleukin-1, a polypeptide also released in the presence of infection. Another recent finding, one Karnovsky terms "rather startling," is that interleukin-1 promotes slow-wave sleep and causes elevation in body temperature (Bahr, Chedid, Dinarello, and Krueger)—and a European investigator has shown that some brain cells produce interleukin-1 when stimulated.

"The circle is closing: slow-wave sleep, cellular immunity, and the nervous system generally have some common aspects."

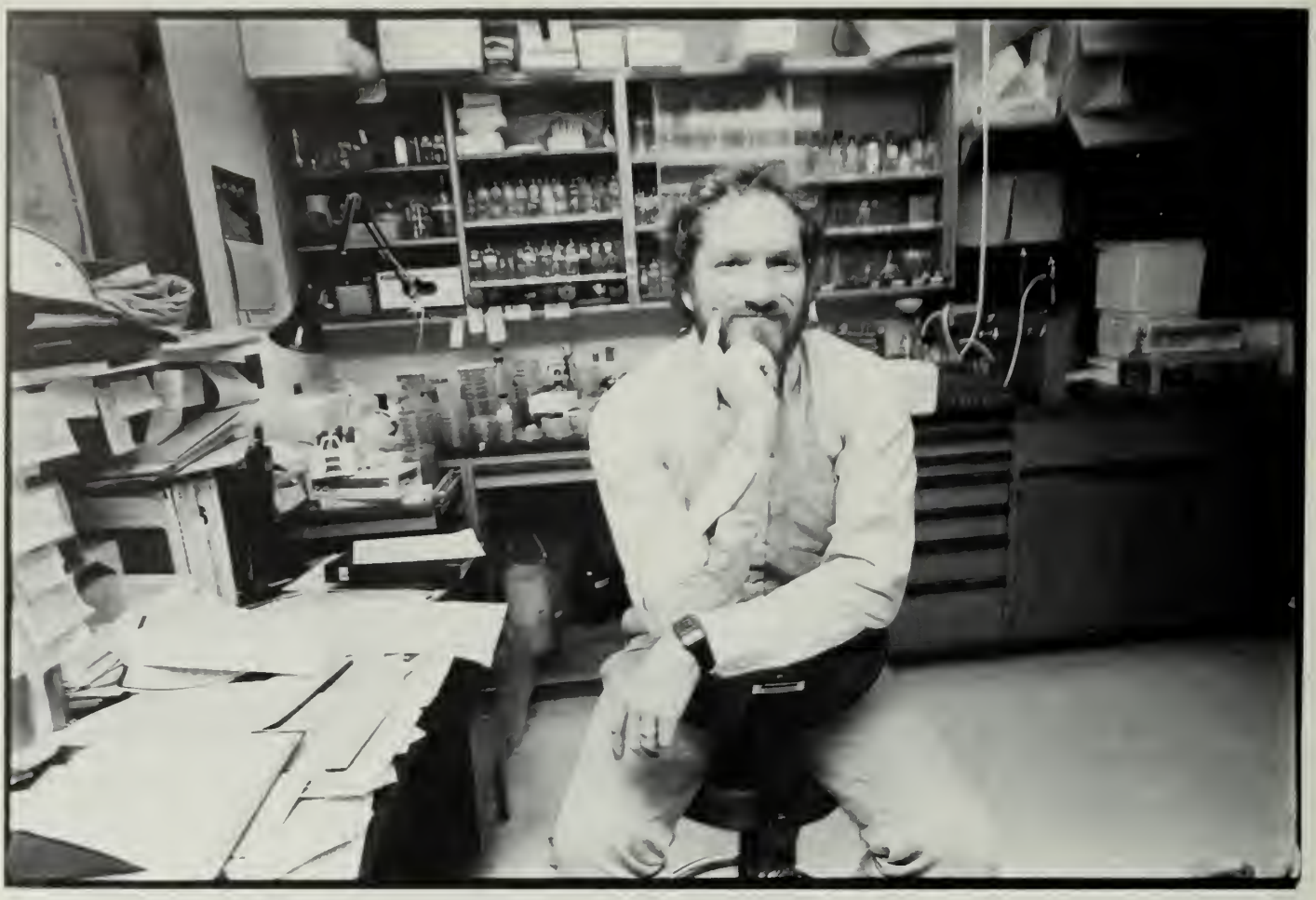
Pressed for a hypothesis about the significance of these findings, Karnovsky says, "If you really want me to go out on a limb, I think that perhaps nature has arranged a whole system of circumstances to combat infection—first to immobilize you with slow-wave sleep, thus conserving your energy; to raise your temperature, thus diminishing spread of infection; and finally, to help turn on the immune system fully, which perhaps is the most savvy thing of all. Maybe slow-wave sleep originated in primordial times as part of this triad of situations that allow one to cope with bacterial infection. How do you prove that, though?"

Karnovsky is also working on two other lines of research. The first is his long-term study of phagocytosis. Recently, he has been looking at the phenomenon of release of oxygen radicals by the cell when the phagocyte's membrane is stimulated—a "powerful mechanism" that helps kill virulent bacteria and may destroy tumor cells, but is also a "two-edged sword," as it poses a potential threat to healthy cells and tissues. "Tom Stossel, at MGH," says Karnovsky, "has just done some beautiful work showing that these oxygen radicals released by phagocytic leukocytes may cause cells to become cancerous—because the radicals may attack DNA and membranes of other cells."

There are some rare clinical conditions, such as Chronic Granulomatous Disease of Childhood, in which the ability to release oxygen radicals is genetically spoiled. "We're very much interested in the basic aspects of the disease," says Karnovsky. "We want to get a good bead on how our white cells keep us as healthy as we are." He is taking a close look at what is happening at the membrane level, and at the enzymes that lie behind the release of oxygen radicals.

Karnovsky is also investigating "how things move around in the cell." He has studied the transport system of an intermediate of glucose metabolism, glucose-6-phosphate, as it moves from the cytoplasm to the membrane (specifically to the lumen of the endoplasmic reticulum membrane), where it is processed and released to the outside as glucose. "When that system is impaired," he explains, "Glycogen Storage Disease is found; the liver becomes full of glycogen and children are very sick. Exactly how that happens is not known, and needs to be."

Manfred Karnovsky is Harold T. White Professor of Biological Chemistry.



John Mekalanos

"In general, we are isolating mutations that change the specific properties of bacteria that make them capable of causing disease."

The one advantage to contracting and then recovering from a virulent bacterial disease, such as cholera, is the long-lasting immunity conferred by the body's response to the live bacteria. Current vaccines for such diseases (dead whole-cell and injected toxoids) have a time-limited effect that may be due to the lack of a local response in the intestine.

With the goal of developing vaccines able to provoke the same long-lasting immunity as the diseases themselves, associate professor of microbiology and molecular genetics John Mekalanos has been studying the genetics of cholera, pertussis (whooping cough), salmonella, *Staphylococcus aureus* (most infamous for causing toxic shock syndrome), and pathogenic strains of *E. coli*. "In general," he explains, "we are isolating mutations that cause a reduction of virulence." These mutations change the specific properties of bacteria that make them capable of causing disease.

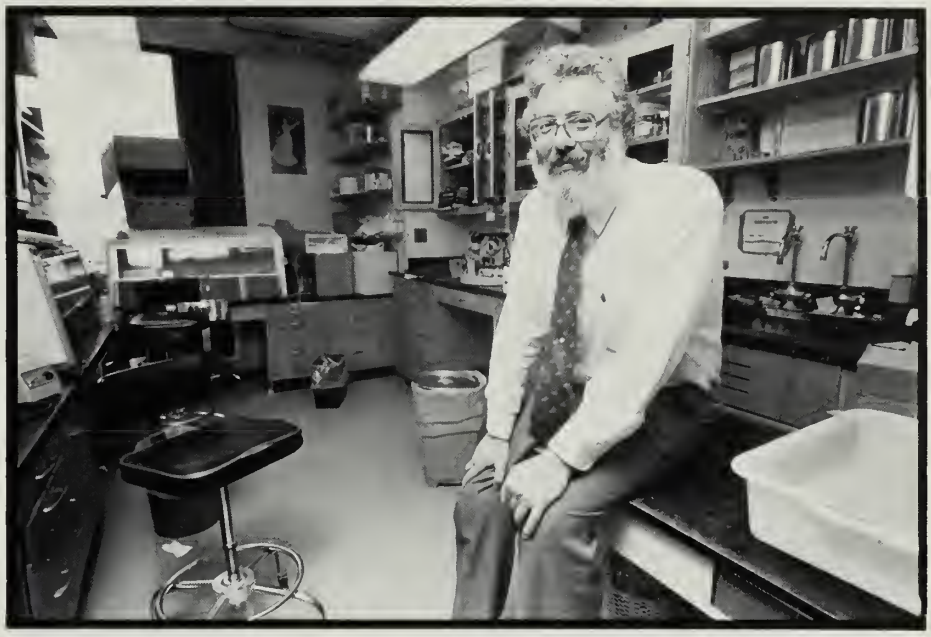
The mutant strains themselves (genetically stabilized by such methods as removal of genes that encode a toxin) may serve as live oral vaccines—but, Mekalanos points out, such a specific approach "doesn't always work with every organism. And it is not a cure-all for all geographical locations." In a second, more elegant approach, he hopes to develop a detoxified protein product (a toxoid), from a gene important to virulence, that will provoke a protective antibody reponse when either injected or taken orally.

Mekalanos's method with each disease is to first isolate mutations in toxin genes in order to identify the genes that control toxicity. He then studies the production and regulation of the protein products encoded by these toxin genes. With that gene product identified, he explains, "you can probably detoxify the protein, characterize it with biochemical analysis, and ultimately produce an antigenic form of the protein that is not deleterious." As a vaccine, that protein would cause a person to develop antibodies that neutralize its toxic form, effectively depriving the bacterium of its toxin in a way somewhat analogous to the original mutation in the toxin gene. The bacterium would "no longer have the luxury of having that gene product available," explains Mekalanos.

Understanding the action of the gene product could also lead to treatment for those who contract the disease. "If we discovered that a toxin causes a certain molecular defect in the cells," says Mekalanos, "then a good pharmacologist might be able to look at it and say, 'ah, this drug might work to help prevent that.' "

Frequently Mekalanos works with pathogens whose effects are well understood, but whose specific gene products have not been identified. "For example, it's well known that *Vibrio cholerae* causes diarrheal disease—but the actual toxins, and all the components the bacterium uses to cause disease, are not known. Only two or three of them have been shown clearly to be involved—the cholera toxin being the major one—but all the other dozens of components have not been studied by a genetic approach."

Thus far Mekalanos has studied the genes responsible for virulence in *Vibrio cholerae*, and has produced two modified, non-toxinogenic forms of the bacteria that may result in a live oral cholera vaccine. He hopes to use this same technique to develop a polyvalent live oral vaccine against a number of bacterial diseases.



Geoffrey Cooper

"We think that these oncogenes play some role in the genesis of the tumor from which they have been isolated."

Within the last few years, scientists have discovered ways of using genes isolated from malignant human and animal tumors to transform (make cancerous) normal cells in culture, and have identified over two dozen oncogenes (genes involved in tumor growth). Several laboratories, including that of professor of pathology Geoffrey Cooper at Dana Farber Cancer Institute, have been using the new techniques—which involve transferring DNA between cells—to probe the role of cellular genetic material in the development of cancer.

The fact that DNA from tumor cells will transform normal cells, according to Cooper, "opens the door to thinking that this is a real change responsible for the cancer. We think that these oncogenes play some role

in the genesis of the tumor from which they have been isolated."

Cooper's work with oncogenes began with studies of the DNA of Rous sarcoma virus. "As the techniques improved," he recalls, "we realized that we could look not just for oncogenes of viral origin, but potentially also for cellular genes with transforming properties."

Three years ago, Cooper's team (including post-doctoral fellows Channing Der and Ted Krontiris) and others determined that some of the genes from human tumors are close relatives of the well-studied *ras* viral transforming genes. A number of researchers were then able to establish that there is no major change in these genes in the tumor cell compared to the normal cell. The differences are of astounding subtlety: the *ras* proteins of the tumor cells contain single amino acid changes that mark the difference between malignancy and normalcy.

Evidence suggests that the *ras* protein—in both normal and cancerous cells—is located in the cellular membrane, and that it is somehow involved in transducing growth signals from a receptor to a target inside the cell. The protein in the transformed cell apparently tells the cell to grow in an unregulated manner.

There is also evidence that the non-viral *Blym* gene—found in B-cell lymphomas in chickens and Burkitt's lymphomas in man—"seems to make a small protein we don't yet know too much about," Cooper says, "although the characterization of that protein is under active study."

The making of a tumor in an animal is a much more complex process than the single-step events Cooper has been observing in culture. "One would think," he says, "that at most these genes play a role in perhaps one step of that process, but are not sufficient to account for all of it."

There are many tumors, he has found, that contain at least two oncogenes. Both the *myc* and *Blym* genes, for example, can be found in all chicken B-cell, and human Burkitt's, lymphomas. *Myc* has been implicated in the first stages of abnormal cell growth, and *Blym* has been implicated in furthering progression of tumor development. Other pairs of oncogenes have been similarly implicated in the growth of other types of tumors.

Although oncogenes are potential targets for early diagnosis or therapy, clinical application is a distant goal. "What you really want for clinical applications," Cooper points out, "is something you can see in a cancer cell that's different from what's in a normal cell, and that you can hopefully direct a drug against. If the oncogene were a separate, new gene, that would be simple, but at a crude level the genomic material of the tumor cell looks the same as that of the normal cell. The normal cell carries the same genes that are present in the tumor."

Another possible diagnostic process is ruled out by the fact that the genes, at least the several that have been well studied, are expressed at similar levels in both the cancerous and normal cells. Scientists therefore can't look for unusual levels of proteins as diagnostic markers.

"The same caveats apply to the notion of therapy," Cooper says. "You obviously can't use a drug or an antibody that will simply wipe out cells that express these genes, as they are involved in normal as well as cancer cells. You can't just knock out any cell that's expressing the *ras* protein, for example, because all cells express normal *ras* proteins. You could try to tailor a drug that would knock out only the mutated form of the protein that's present in cancer cells, but since those mutations are single amino acid changes, it's not obvious how to do that. And although they are not totally random, the amino acid changes are different in different tumors."

Cooper and colleagues are continuing to isolate oncogenes for the same sort of painstaking analysis—"to answer the basic question," Cooper says, "of what differentiates tumor cells from normal cells at the molecular level."

Donald Coen

"What do drug-resistant mutants tell us? To paraphrase Freud, they're the royal road to determining the mechanism of the action of the drug."

The recent advent of antiviral drugs—licensed so far in this country for use against the flu and members of the herpes family—raises questions about how such drugs work, and about the likelihood of fostering drug-resistant mutations with their use. These questions and others are being addressed in the laboratory of assistant professor of pharmacology Donald Coen, where investigators have been studying mutations of the herpes simplex virus (HSV), and have also started looking at cytomegalovirus, a less well known but pervasive HSV relative that is usually asymptomatic. Both viruses can have severe effects on infants and immuno-compromised patients.

"What do drug-resistant mutants tell us?" asks Coen. "First, to paraphrase Freud, they're the royal road to determining the mechanism of the action of the drug. If you can isolate a drug-resistant mutant, you know right off the bat that the drug actually is selective against the virus. You then try to identify a gene in which mutation has occurred, which in turn identifies a gene product important for the action of the drug." Coen has been working with two of the handful of antiviral drugs used against herpesviruses: araA (vidarabine) and acyclovir. Both attack the virus in its active state; no drug has yet been shown to eradicate latent herpesviruses from the body.

Following up on work he began several years ago as a post-doctoral fellow in the lab of Priscilla Schaffer at Dana Farber Cancer Center, Coen is using two HSV genes to compare the viral and cellular processes of

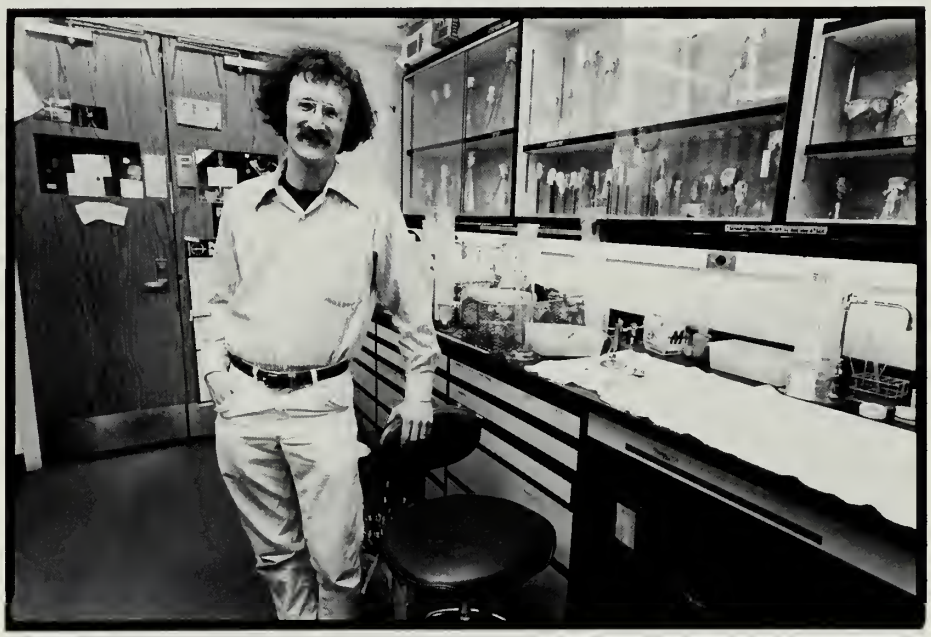
replication and gene expression. Both genes have been shown to mutate to confer drug resistance.

To study replication, Coen is focusing on herpesvirus DNA polymerase, the enzyme that catalyzes replication of viral DNA. Coen and co-workers have found that the basis for the action of araA is that it more readily inhibits, or is incorporated by, the virus polymerase over the cellular polymerase. That same mechanism, they have also found, is partly responsible for the antiviral action of acyclovir—a finding in line with results based on biochemical research at Burroughs Welcome Company. Similar work has been carried out by Lowell Schnipper, Clyde Crumpacker, and colleagues at Beth Israel Hospital, and by scientists at Cambridge University.

"We're interested in herpesvirus DNA polymerase," Coen explains, "because it is an extremely good model—both for other viral DNA polymerases and for our own cellular DNA polymerase. Graduate student Jim Gibbs and technician Margie Retondo (now HMS '88) of our lab have just finished sequencing the polymerase gene, so we now presumably know every amino acid in the protein. We've also isolated many mutants that affect different properties of the polymerase. Recently graduate student Henry Chiou of the lab has mapped several mutations that make the virus either resistant or hypersensitive to a number of drugs, some of which are antiviral agents. Since these drugs mimic normal polymerase substrates, we can now ask which polymerase amino acids are involved in substrate recognition."

To study viral and cellular gene expression, Coen has been using the HSV thymidine kinase gene. He has been comparing the ways the gene is expressed as part of the viral chromosome infecting the cell, and as a piece of DNA from the virus introduced into cells by itself. "In the first case," he has found, "it's under a particular regulatory program. In the second case, it behaves pretty much like a cellular gene, and is expressed all the time."

In one study, in collaboration with Steve McKnight of the Carnegie Institute in Baltimore, Coen and technician Laurel Leslie have studied mutations in the promoter region of the thymidine kinase gene. "Promoters are sequences upstream of genes which control the level of their expression," explains Coen. "A lot of what we know about promoters has actually come from studies of the HSV thymidine kinase gene; even though it's not a normal cellular gene, it's been easy to study." These studies could lead to another avenue to be exploited for therapeutic purposes.



Coen is also asking whether mutants that are resistant to one drug are as likely to be resistant to other drugs. There are drugs, he has found, that are fully effective in the laboratory against araA-resistant mutants. "Acyclovir is about to be offered to lots of people," he points out. "If resistant viruses should arise in the clinic, it would be helpful to have alternative drugs that are active against the mutants."

Ursula Dräger

"Nature is economical, in particular during embryonic development: it would not consistently synthesize melanin pigment in the early embryo unless the pigment fulfills a function."

Associate professor of neurobiology Ursula Dräger studies the normal and abnormal workings of the visual system at the cell biology level. Using mice with genetic mutations that affect the development and functioning of the eye, she has been identifying specific components implicated in inborn neurologic defects and in aging.

Among Dräger's recent findings are that the optic projections which form the basis of binocular vision develop in the early embryo, and are not a consequence of competition between the two eyes; that melanin (black pigment) binds calcium, a capacity that may play an unexpectedly fundamental role in neurological development and health; and that the fast physiological changes accompanying light and dark adaptation in photoreceptors can be detected with antibodies, discovered in her lab, that label phosphorylated sites.

It has been known for some time that animals with less than normal amounts of melanin have a number of neurologic defects. These defects mostly affect vision, and sometimes impair hearing. The most obvious neurological symptoms in the human albino, for example, are poor visual resolution, lack of binocular vision, squint (strabismus), and uncontrolled eye movements (nystagmus). "Because these defects are not due to light scatter in the unpigmented eye," Dräger explains, "but reflect faulty neuronal connections in the eye and brain, they point to unknown functions of melanin in addition to the known photoprotective function."

Pigmentation of the eye, Dräger points out, is formed in utero—long before there is any need for photoprotection. "You think pigment is needed for light screening," she says, "but this embryo won't see light for four weeks, and doesn't have photoreceptors yet, so there is no earthly reason why it should have pigment. Moreover, if you look at a human, mouse, or whale embryo—any embryo that size, regardless of the eventual size of the animal—the eye becomes pigmented. Nature is economical, in particular during embryonic development; it would not consistently synthesize melanin pigment in the early embryo unless the pigment fulfills a function."

Scientists have long assumed that because binocular vision seems to be phylogenetically younger than monocular vision, it must be ontogenetically formed later. In other words, because the more sophisticated binocular vision of the primate is high in the evolutionary chain, compared to the monocular vision in fish, for example, one would assume that its development in the embryo comes at a later stage than monocular vision.

Dräger's recent experiments have proved this assumption wrong. With classical thymidine labeling techniques, and other techniques developed in her lab, Dräger has charted in the mouse embryo the time course of the formation of the nerve cells that mediate binocular vision later in life. She has found that "the neuronal machinery that enables binocular vision is formed at the earliest stage of eye development. Curiously, at exactly the time this system is established in the embryo, the eye becomes pigmented—and the albino mutant tells us that lack of pigment results in defective binocular vision. What is the pigment doing there at that time?"

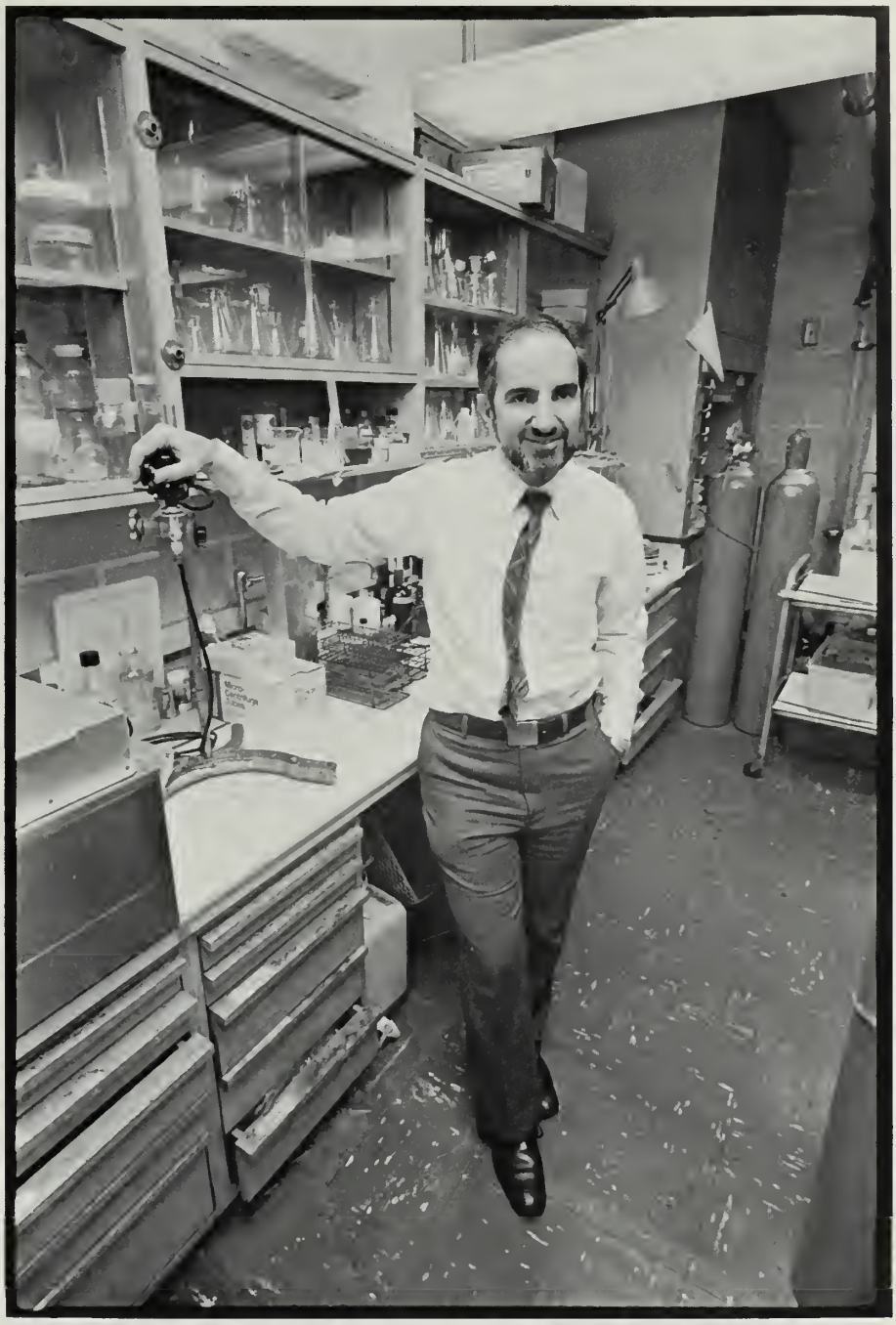
She has found clues in seemingly unrelated experiments. To determine where calcium—an ion of almost universal significance—binds in the tissue, she developed a novel technique. After removing calcium from histology sections, she replaced it with radioactive calcium, and found that melanin binds large amounts of calcium. Her working hypothesis is that

"the calcium-binding capacity is the unknown property of melanin pigment, and that the neurological defects reflect a defect in calcium regulation."

In another project, Dräger and colleagues have developed monoclonal antibodies that label neurofilaments, a main component in neurons. Some of these antibodies, it turns out, label phosphorylation sites on the heavy subunit neurofilaments. In one experiment, the investigators cut axons in the brain and, according to Dräger, "suddenly the cells lit up in reaction to the injury"—as the cells put phosphates on the neurofilaments. These antibodies, Dräger and her colleagues have concluded, "can be used to detect damage in neurofilament-rich neurons at a very early stage, long before they degenerate."

"People don't have the faintest idea," says Dräger, "what neurofilaments are good for, or why they are phosphorylated. The only conclusion we can draw is that this particular pattern of phosphorylation of the heavier weight neurofilaments indicates that something bad is happening to the cell."

In trying to turn on the phosphorylation of neurofilaments, Dräger found her antibodies labeling sites in the photoreceptors of the retina. When the rhodopsin molecule in the photoreceptor sees light, it becomes phosphorylated as it turns from purple to yellow. "Normally you use antibodies to see structures," she explains. "What we saw in the photoreceptors was fast physiological changes." This serendipitous discovery may provide novel tools to study dark adaptation defects in hypopigmented mice, as well as reveal subtle defects in aging cells.



Alfred Goldberg

As a first-year HMS student 20 years ago, Alfred Goldberg had no idea that a simple question—"How does a muscle become smaller after the nerve to it is cut?"—would lead him out of medical school, take him into the molecular biology of the process, and eventually yield answers with profound biochemical, clinical, and industrial applications. "The answer

turned out to be excessive protein breakdown," recalls Goldberg, now professor of physiology. "No one understood the biochemistry or regulation of protein degradation, a process all cells carry out. This interest grew into a research project, a leave of absence from HMS, a Ph.D. thesis, and a life's work."

Goldberg's studies now "range from biochemical questions best studied with pure enzymes and in bacteria by genetic approaches, to physiological studies we can discuss with clinicians and surgeons. It's funny that as our work gets more basic, it's also getting more relevant to medical practice."

One major theme of Goldberg's work is the biochemical question of how cells rid themselves of highly abnormal proteins—a problem that has also proved to be of critical importance to the recombinant DNA industry. Goldberg views the process "as a cellular sanitation system to get rid of inactive, potentially harmful proteins that may result from genetic mutations, biosynthetic errors, or damage to cell constituents."

Industry became interested in Goldberg's work with the finding that protein degradation can interfere with the recombinant DNA technique of producing proteins—such as insulin and certain growth hormones—in bacteria. "In many cases, the bacteria rapidly degrade the foreign polypeptides," explains Goldberg. Investigators and industry are now using strains defective in protein breakdown, found by his lab, to increase the yield of cloned proteins.

Recently Goldberg and graduate student Steven Goff discovered that the appearance of large amounts of foreign proteins causes cells to make more degradative enzymes (proteases). "So bacteria, and presumably mammalian cells, have evolved protective mechanisms against useless polypeptides," Goldberg explains. "How they do that is interesting for us scientifically: how do the bacteria recognize these proteins as being different, and how do they destroy them without affecting normal proteins?" The answers are providing ways to produce strains defective in the control of the production of destructive enzymes, which could, like the strains with defective proteases, be used to increase the yield of cloned proteins.

Physiological studies in Goldberg's laboratory have shown that muscle size is determined by the balance between rates of protein synthesis and breakdown. This finding has relevance to growth, and to conditions in which muscles atrophy from rapid protein degradation—such as muscular dystrophy, diabetes, and infection. "We've been studying how this process occurs and how it may be retarded," explains Goldberg. "This area is turning out to have a number of applications in the care of patients with surgical trauma, renal failure, and burns."

"The fundamental question may be not just how the cell degrades foreign proteins, but why it doesn't digest itself."

Goldberg is also interested in how the loss of tissue protein is activated in disease states. With postdoctoral fellows Julie Fagan and Vickie Baracos, he has recently shown that the polypeptide interleukin-1, a macrophage product that activates white-cell defense mechanisms and triggers fever, specifically causes the breakdown of muscle protein. Understanding that mechanism might help treatment of the wasting of tissues in chronic diseases and generalized infection—"and maybe even the cachexia seen in burn patients and in cancer," Goldberg says.

One of the major findings in Goldberg's laboratory in recent years is that there is a second pathway for protein breakdown, in addition to the lysosome (an organelle once thought to be the sole site of protein breakdown), and that the separate pathways serve different physiologic functions. Fagan and Waxman have also just discovered that there are multiple nonlysosomal pathways. The lab is now probing the biochemical requirements for recognition and degradation of different types of damaged proteins.

The lab has found one degradative system that requires metabolic energy in the form of adenosine triphosphate (ATP). "On thermodynamic grounds, that energy requirement would not be expected," Goldberg says. "We've discovered a new kind of enzyme, ATP-dependent protease, that we think is critical in this process and for life." This system, which selectively degrades incomplete, mutant, or damaged proteins, is the main route for protein breakdown in rapidly growing cells.

Goldberg's group, in particular principal research associate Lloyd Waxman, has shown that the ATP-dependent protease exists in bacteria, mitochondria, and mammalian cells. The lab now plans to look at how this novel enzyme makes use of ATP, and has also been looking at how cells with the enzyme avoid destroying useful cell proteins. "That may be the fundamental question," Goldberg says, "not just how the cell degrades foreign things, but why it doesn't digest itself—and how these potentially destructive enzymes are controlled normally, and activated under stressful conditions."

About the clinical application of his work, Goldberg says, "There is no question that the immediate application is conceptual. We are only starting to understand protein turnover in normal cells, and why some proteins have short half-lives and others are stable. For a large variety of diseases, there is excessive breakdown of tissue proteins. Rational therapy probably must await more precise physiological and biochemical knowledge about that process."

Jonathan Seidman

"According to common folklore, the heart sends out love—but really it sends out atrial natriuretic factor, a potent diuretic."

The discovery of atrial natriuretic factor—a hormone released by the heart that regulates fluid balance in the body—by Canadian researcher DeBold several years ago sparked interest in many fields. Perhaps the finding would lead to treatments for high blood pressure. Perhaps an understanding of the pressure- or volume-sensing mechanism could illuminate the baffling workings of other receptors, such as taste and smell.

A number of groups, including the Harvard team of Jonathan Seidman, Christine Seidman, and Kenneth Bloch, and collaborators at Massachusetts General Hospital, set about studying the action and architecture of the hormone. "The heart turns out to be more than a pump," explains Jonathan Seidman. "It is an encodrine organ with an important role in determining blood pressure. According to common folklore, the heart sends out love—but really it sends out atrial natriuretic factor, a potent diuretic."

In January of last year, two groups published the structure of a 24-amino-acid peptide hormone of the mouse and human. Recently, working backward from the protein to the DNA—like using the house to determine the blueprints—the Harvard team has determined that the hormone is much larger than originally thought. "We now know," explains Seidman, "that the smaller molecule comes from a protein originally 152 amino acids long that's chewed down to 28 amino acids." This finding puts atrial natriuretic factor in the same class as large peptide hormones such as insulin or parathyroid.

"The question is, where does that breakdown occur?" asks Seidman. "It turns out that the storage form of the molecule is 126 amino acids, and that's what gets released from the heart cell in response to pressure changes. Now we can start to study the mechanisms that cause release."

The team made its finding with recombinant DNA technology. "When you know the amino acid sequence," Seidman explains, "you can make oligonucleotide probes that bind specifically to messenger RNA. So you make a large bank of plasmids, or cloned probes, that correspond to every messenger RNA in the atria, and then screen that bank of plasmids with these oligonucleotides." The investigators were then able to predict precisely the structure of the whole protein from which the smaller peptide is derived, and to determine that two percent of the messenger RNA in the upper chamber of the heart encodes atrial natriuretic factor. They also found, by looking for the messenger RNA elsewhere, that the peptide is either not expressed in other tissues of the body, or is expressed at much lower levels.

Two hospitals—in San Francisco and England—are currently doing clinical trials in the treatment of high blood pressure with the smaller peptide. One problem with this application, among others, points out Seidman, "is that because it is a protein, it must be injected to be clinically useful."

Seidman is now making single-cell cultures that cause a specific release of the hormone. "Then we'll be able to ask specifically what are the mediators of this release mechanism," he says. "Eventually one may be able to identify the pressure receptor, and use a biochemical approach to determining the structure of this pressure receptor molecule. One might be able to find drugs that would bind to the pressure receptor—the simplest possibility—and then change its sensitivity."

Jonathan Seidman is associate professor of genetics, Christine Seidman is a cardiology fellow at MGH, and Kenneth Bloch is a post-doctoral fellow.

A Lab of One's Own

Six Faculty Members Ponder the Woman's Place

When we first considered covering the subject of women in research, we consulted Eleanor Shore, associate dean for faculty affairs and a member of our editorial board. She directed us to the Office for Academic Careers and the Joint Committee on the Status of Women, and to a number of female faculty members—and contributed an overview of HMS's progress in hiring and promoting women basic scientists.

In the pieces that follow Shore's, an assistant professor of pediatrics describes a day in her life of juggling parenting, clinical work, teaching, and research; an associate professor of physiology and biophysics recalls the evolution in attitudes of her male colleagues; a neurobiologist writes about combining motherhood and lab work; and a psychiatrist at Harvard University Health

Service and an associate professor of physiology and biophysics both consider the importance of role models.

Shore's research for her piece included combing HMS's Official Registers over this century for the names of women in basic science, with the help of Clyde Evans, director of the Office for Academic Careers. "Even though we were focusing on women," says Evans, "we feel it is important to note that the history of HMS has been greatly enriched by the contributions of many minority scientists and physicians over the years. The record of these accomplishments is more difficult to retrieve because information was simply not recorded along ethnic lines until recently. Nevertheless, we feel that story ought to be told, and we hope to do so in the future."

The number of women faculty members has increased dramatically over the last 16 years— now up to 23 percent of basic science faculty positions— but women still don't move to the upper rungs of the promotion ladder in the same proportion as men. Efforts at HMS to diminish the hurdles these women face are coordinated by the Office for Academic Careers and the Joint Committee on the Status of Women. Opened initially in response to urgings by women and minority groups, OAC offers advice to all post-doctoral fellows and junior faculty on applying for grants (including a workshop on NIH grants and review systems to be held this fall), and sponsors the Office for Parenting, a networking and information resource. JCSW holds discussions at which senior women explain to their younger colleagues the requirements for promotion, and sponsors special events, such as a symposium on Science, Gender and the Research Process, held in April.

Asked recently for the causes of women's slower career progress, Clyde Evans cited the shouldering of more than half of household and family responsibilities; absence of role models and mentors; feelings of isolation; and a tendency to carry a disproportionate share of teaching and committee work, which distracts from research— a critical factor in promotions. (Women faculty members are deluged by requests from committees, which want representation from women and minorities, and by female students looking for mentors.) Evans also noted that proportionately fewer women than men apply for fellowships.

"These factors may be as much symptoms as they are causes," Evans adds, citing a recent study of the National Academy of Sciences that found differences in promotions of male and female junior faculty even when they were closely matched by subfield, prestige of the department from which they received their Ph.D., and years since obtaining doctorate. Women lagged behind men in faculty promotions regardless of marital status, presence or absence of children, and primary work orientation (research or teaching). "Even though the NAS findings and my own observations seem to point in different directions," Evans concludes, "I believe we are both on to something important."

Looking into two of the major funding sources, we found programs that help the scientist/mother reenter research after a hiatus in her career. This year the National Science Foundation earmarked $2.5 million to fund projects proposed by women entering or returning to science. NIH's Investigator Research Award, though not exclusively for women, is also designed for those reentering research or switching fields. In addition, the report of the recent National Institute of Child Health and Human Development Workshop on Clinical Research Careers for Women (chaired by Carola Eisenberg, HMS dean for student affairs) recommends that NIH establish part-time fellowships and allow short-term deferment of fellowships and career development grants at critical times for parenting.

When they make it to high-level faculty positions, women can feel isolated from their peers. At the symposium on Science, Gender and the Research Process (attended almost exclusively by women), a full professor at University of Massachusetts Medical Center replied to a question about her female colleagues: "There aren't a lot of women scientists at my level." At HMS, women scattered among the hospitals and in the Quadrangle may not have easy access to one another— and they often feel excluded from the informal networking their male colleagues enjoy. "Before I married I felt awkward approaching a male coworker and saying 'Let's have lunch,' " an associate professor says. "Also, women can't participate in casual talks in the men's room or on the squash court."

Despite these continuing problems, the situation for women basic scientists at HMS has improved so much that at least one young associate professor says her sex is simply not an issue, and that it doesn't matter to her whether her colleagues, role models, and mentors are men or women. On the flip side of that coin, though, third-year student and fellowship award winner Terri Young says she didn't identify herself as a future researcher until recently— because none of her teachers or lab directors were women, blacks, or members of other minority groups. "It will be some time before there's an equitable distribution of all types of people in medicine," she says. "But that takes time. There's nothing you can do about history."

Making Progress

by Eleanor Shore

When I entered Harvard Medical School in 1951, there was one woman basic scientist*, an assistant professor, on the voting faculty; at the time of my 30th reunion this spring, there were 86 with that rank or higher (including associate and full professors). This increase is 8,600 percent, better than the growth of the GNP, the rate of population increase, or any other indicator I can think of.

In the first decade of the 20th century representation of women was nil: a small number received some training, but faculty titles at any level were non-existent. As I found in researching "The Invisible Faculty" for the Summer 1983 *Bulletin*, the second decade didn't start out much better. Harvard University president A. Lawrence Lowell wrote on September 29, 1910, to Ernest Southard, Bullard Professor of Neuropathology, who wanted a better title than custodian for Dr. Emma Mooers: "I brought up the question of Miss Mooers' appointment before the Corporation, and they would be very glad to change her title to any other that would be satisfactory to her, which does not imply that she holds, or that women are entitled to hold, a Fellowship in the Medical School."

HMS dean Henry A. Christian wrote to President Lowell on June 20, 1911, "Since the nominations from the faculty for annual appointments were sent in, I have discovered that the person nominated for Research Assistant in Biological Chemistry, Willey Denis, is a woman. If you will recall, there was considerable discussion occasioned a year ago in regard to the nomination of Dr. Mooers for a fellowship, and the feeling in the faculty is strongly against appointing a woman to be in a teaching position. I have just been talking with Dr. Folin about this matter and it seems satisfactory to him to change the title from Research Assistant to Technical Assistant and to omit the name from the roster of instructors and simply have her name appear on the payroll as do other technical assistants, stenographers, etc."

Despite this unpromising correspondence, the decade ended better than it began with the HMS appointment in 1919 of Alice Hamilton, M.D., as assistant professor of industrial medicine. Because her appointment was in industrial medicine, with primary academic responsibilities in the Harvard-MIT School of Public Health, it cannot be regarded as a basic science position—but it was the first professorial title for a woman anywhere in the university. No woman in basic science would hold even an assistant professorship for another 30 years.

The first two women research fellows, both physicians in the Department of Pathology and fellows of the National Research Council, were appointed in 1925 and 1929, and a third woman physician, Myrtelle Canavan, was appointed curator of the Warren Museum in 1923—despite one faculty attempt to cap the title with a modifying "assistant." In the following decade, the first two women basic scientists were named research associates, while seven others became research fellows. In 1938 Caroline A. Chandler, M.D., was appointed not only research fellow in obstetrics but also assistant in bacteriology. None of these women survived the faculty selection process to become any level of professor, and their unfamiliar names appeared and disappeared like the smile of the Cheshire cat.

By the 1940s women were receiving a wider variety of non-voting faculty appointments. Ann Kuttner, Ph.D., became lecturer in bacteriology and immunology. In 1945, the same year HMS first admitted women students, Helen W. Deane, Ph.D., and Harriet Maling, Ph.D., became instructors in anatomy and pharmacology, respectively. Shortly thereafter, Esther Hardenbergh, A.M., and Elizabeth Leduc, Ph.D., became instructors in physiology and anatomy, respectively. By the end of the decade, Helen Deane and Barbara W. Low, both Ph.D.s, were associates, respectively, in anatomy and physical chemistry, the highest rank for women basic scientists in the first half of the 20th century.

In 1950, at the beginning of the second half of the century, the unthinkable happened: Barbara Low, who had been recruited from Oxford University to study protein crystals by X-ray diffraction, was named assistant professor of physical chemistry in the Department of Biophysical Chemistry. The following year, Helen Deane was promoted to assistant professor of anatomy, and it seemed the clouds were beginning to break.

The fact that there was a woman basic scientist on the faculty when I entered HMS as part of the sixth class to admit women, and the appointment of a second woman to faculty rank in my first year, were regarded as very positive signs. There was a general assumption among the eight women in my class that barriers were coming down. Few of us realized how extraordinary those first appointments were, or how long it would be until these women had any significant number of peers. It was not for another two decades that women's representation in the basic sciences would reach double-digit figures.

By the end of that decade, one more woman was assistant professor of anatomy, Helen Padykula, Ph.D., appointed in 1959. However, Low and Deane were no longer in the register, so the total number of women professorial appointments in the basic sciences now stood at one, as it had at the beginning of the decade. (Progress in clinical departments was somewhat better. Grete Bibring became assistant professor of psychiatry at Beth Israel Hospital in 1951, was promoted to associate clinical rank in 1955, and attained full professorship in 1961; Harriet Hardy became assistant clinical professor of preventive medicine in 1955, and associate clinical professor in 1958; Elizabeth Zetzel became assistant clinical professor of psychiatry in 1957.)

In February 1960, Elizabeth Hay, M.D., then an investigator of limb

*Basic scientists include those women with appointments in the preclinical basic science departments and women Ph.D.s in clinical departments.

regeneration in amphibia, came from Cornell Medical College to become assistant professor of anatomy. By 1964 she was the Louise Foote Pfeiffer Associate Professor of Embryology, and in 1969 she became the first woman to hold a full professorship in a basic science department. She had become a leading investigator in the field of extracellular matrix of connective tissue and its relation to embryonic induction and differentiation. Others who set the pace for the 1960s were Jean M. Marshall, Ph.D., who became assistant professor of pharmacology in 1960, and Olive Smith, Ph.D., assistant professor of biological chemistry in the Department of OB-GYN at the Free Hospital for Women that same year. By 1969-70, there were six women basic scientists with voting faculty ranks. (There were another 12 women physicians, doing clinical medicine or research, in clinical departments.)

Real progress for women basic scientists did not come until the 1970s. By 1980 there were three women professors, nine associate professors, and 27 assistant professors (see table). Just five years later, the basic sciences boast six women professors, 22 associate professors, and 58 assistant professors. Why this relatively sudden escalation? Is it an increased awareness of women's potential scientific contributions? External pressure to provide equal opportunity? Better scientific preparation of women in high school and college?

The fact that the number of women basic scientists on the voting Faculty of Medicine has increased from four to 86 in 16 years should surely go down in the annals of HMS as one of its significant accomplishments. No academic institution can afford to restrict its selection of scientists to one-half the available talent pool, and HMS has clearly begun to tap this newly recognized resource. Before becoming too self-congratulatory, however, we must ask whether the progress has been good enough. Are women now represented in numbers consistent with the corresponding pools of available Ph.D.s? The National Research Council's Doctorate Record Files indicate that 14.9 percent of Ph.D.s in the biological sciences were awarded to women between 1920 and 1972; 22 percent between 1973 and 1977; and 27.4 percent between 1978 and 1981. A rough comparison would suggest that HMS is doing very well at the assistant professor level, slightly less well at the associate professor level, and not too well at the professor level.

One curious comparison that emerged during this analysis is that the representation of women basic scientists is more than twice that of women M.D.s in clinical departments at each faculty rank. One might speculate that patient care, added to teaching, research, and sometimes family responsibilities, may make an academic career one step more difficult to encompass for women physicians in clinical departments. All the factors are not known, and this difference clearly deserves careful study.

Are women less academically productive than men, and if so, why? A 1979 NRC study, "Doctoral Women Scientists in Academe," indicated that women had published fewer journal articles than men, and that their papers were cited less often. Women were less likely to be married, and more likely to describe themselves as immobile for the purposes of job change.

Is women's lower rate of publishing due to greater family obligations, less access to grant support, fewer assigned graduate students, or some other, unidentified, factor? The NRC study suggested that only 12 percent of married men had wives who had been employed full-time or almost full-time since marriage, while 90 percent of married women had husbands who had been employed full-time or almost full-time since marriage. The NRC study did not gather data on access to research facilities, graduate students, and research assistants, but suggested these be studied.

The NRC study also did not address the question of how many children of what ages their women scientists had, nor did it touch upon flexibility of research departments in accommodating transient periods of increased family responsibility. At HMS this issue is being addressed by the Joint Committee on the Status of Women (joint with the schools of Public Health and Dental Medicine), and the Office of Academic Careers. The fact that the six women basic science full professors have an aggregate number of one child suggests that the dual role of parent and professor is not easily encompassed—and requires considerable energy and ingenuity on the part of the individual woman, her spouse, and the institution. Issues of maternity leave, childcare assistance, and peer support are under scrutiny. Surveys of women faculty to identify other factors contributing to the difficulty for women in leaping the last hurdle are in the final planning stage.

Future representation of women on the basic science faculty consistent with the number of women in the general population (as opposed to the Ph.D. population) rests on a series of dilemmas and decisions which occur long before the issue of faculty appointment arises. One myth after another about women's math and science abilities has been dispelled after careful analyses. A two-year study funded by the National Institute of Education, published in 1980, demonstrated that 13-year-old females start their high school mathematics career with the same ability as males; it is the degree of participation in math courses that differs most significantly over the next four years. Why do fewer women than men take advanced science and math courses in high school? Why do fewer women concentrate in the sciences in college? Why do fewer women enroll in science Ph.D. programs after college? Answers to these questions are important if the pool from which academic institutions draw is ever to include all the potential talent.

Despite the seeming fascination with numbers and percentages in this account of women in HMS's basic sciences, such an analysis is strictly *in vitro*. Making it *in vivo* requires a translation of the numbers into the lives of individual women scientists. The *Bulletin* has asked five women to do just that; their accounts follow. □

Women Basic Science Faculty (including Ph.D.s in clinical departments)

	1980		1985	
	Number of Women	Percent of Basic Science Faculty	Number of Women	Percent of Basic Science Faculty
Professor	3	(5.2%)	6	(9.2%)
Associate Professor	9	(17.0%)	22	(20.8%)
Assistant Professor	27	(22.0%)	58	(28.0%)
TOTAL	**39**		**86**	

A Day in the Life

by Orah S. Platt

TRADITIONALLY, THE ACADEMIC physician has been the man who excells in three roles—clinician, scientist, and teacher. These outstanding individuals are our memorable professors, mentors, and colleagues. But times change, and a new three-pronged academic physician is emerging—the clinician/scientist/mother (C/S/M). Although such extraordinary pioneers have existed for generations, the ranks are just now beginning to fill. I am lucky enough to be able to observe a number of such successful C/S/Ms at close range.

You know at least one such woman. She appears at 8:30 A.M. looking like something out of *Vogue* (actually in something homemade from *Vogue Patterns*), having already orchestrated a three-course family breakfast complete with stimulating conversation and background of carefully selected classical music. The well-scrubbed, color-coordinated (and very intelligent) children are all packed off to school, brown bags brimming with whole wheat molasses bread sandwiches and carob brownies. In the lab she completes the simple yet elegant experiment that satisfies the last trenchant question of perceptive "Reviewer B" of the *Journal of Clinical Investigation*. Lunch is a light fresh fruit salad from the Dana-Farber cafeteria eaten at chief resident's rounds, where difficult diagnostic and management cases are discussed. Here she deftly synthesizes the perplexing case presented by the sleepy intern, bolsters the confidence of the defensive house staff, and skillfully lays the groundwork for the chief of medicine so that he trips right into the insightful diagnosis.

During afternoon office hours she sees five patients with an HMS II who is just starting Introduction to Clinical Medicine. This wide-eyed student witnesses a dazzling display of calm clinical competence, perceptive psychology, and warm personal interaction. Pathophysiology comes alive, physical findings become obvious, and talking with patients seems quite natural. A few terse notes later she's back in the lab to set up for tomorrow's work. Stuffing a manuscript draft and a review for the *Journal* into her briefcase, she's off to ballet class and the soccer field to pick up the kids. They bubble on all the way home, full of the gory little details of mischief at recess, new scatologic limericks, and impossible multiplication tables (base 7). Four quick salmon steaks on the Jenn Air later, she puts in an hour of "quality time" with each child, going over homework, smoothing ruffled feathers of the day, and supervising bedtime.

A new three-pronged academic physician is emerging: the clinician/scientist/mother.

At nine o'clock there is plenty of time to knock off the review, complete the revision, flip through a couple of journals, straighten up the kitchen, throw a load of clothes in the washer, work on a tricky Bach two-part invention—all the while giving "undivided" attention to her incredibly handsome husband.

I have been trying to be one of these star-quality C/S/Ms for years, but it doesn't seem to be working out for me. In the morning I drag out of bed and try to shovel the debris off the kitchen table to make room for a few cups and plates. Breakfast is always a simple affair—a choice of boxes, served complete with bowl and spoon. (When we eat out, my son, Alex, is always surprised that the silverware and napkin come before the food.) Then I try to convince Alex that the "tuna salad on a frank roll" they're serving at school sounds great. He concedes (not relishing the peanut butter and jelly alternative), and as he stuffs the dollar into his pocket, I get a chance to scan him to see if the holes and smudges are discreet enough for school.

I'm late for work (the missing sneaker cost me half an hour). There are already three messages on the board, and I haven't walked into the lab yet. Determined to finish an experiment I started a month before, I decide to pour my gels first, and then answer the messages while the gels polymerize. As I set up the glass tubes in the rack, my research associate ("Magic Fingers") fills me in on the progress of her work. While we discuss a series of followup experiments, I prepare the gel mixture and quickly pipette it into the tubes before it polymerizes. Now the tube gels should stand for an hour before samples are run on them.

The first two phone messages are from clinical referrals, but the callers aren't available. The third is a reminder that I have three students scheduled to begin ICM in the afternoon, and that a patient is lined up for us. The callbacks done, I am ready to run my gels. Magic Fingers watches as I bring the tubes to the sink to pour off the few drops of liquid from the tops of the gels before loading on my samples. But it isn't a few drops; the gels haven't polymerized at all, and the contents slip down the drain. Magic Fingers is always supportive when my samples are contaminated, my flasks break, my columns drip between tubes, or I run my gels upside down. I reciprocate by trying not to ruin her experiments too often.

I have an hour before lunch to catch up on correspondence before meeting with the students. My dictation is interrupted by a caller who strikes terror in the heart of the C/S/M: the school nurse. "I just thought I'd let you know that Alex stuck a paperclip into an electric socket. The burns on his fingers don't look too bad—sort of blackish, not painful at all. He's breathing fine now, there was only a small fire in the classroom and he's back in class." This is the same school nurse who made me pick him up immediately when he said he had a headache during math. As I rush off to Alex's school, I can't help thinking about my residency training at the Shriner's Burn Institute, and the terrible high-voltage shock cases I'd worked on (fine on the outside, seared on the

inside). Fortunately, the black stuff washes off Alex's fingers, and the burn in the school's rug is small—but the smell of burning rubber in the classroom will last a few days.

I apologize to my new ICM students for being late, and set off to see their first pediatric patient. I know how uncomfortable the students and families feel under these circumstances, so I try especially hard to be non-threatening and appreciative of this family's generosity. The opening patter of introductions and explanations goes fine, but within a few minutes the family is sobbing, and the four of us are out in the hall feeling terrible. The alternative is to use your own kid as an ICM patient. Last year I palmed him off as Alexander Shattuck, age eight (he was five at the time and enjoyed the subterfuge). I had hoped to illustrate the importance of using growth charts as part of the physical exam. Unfortunately, while I was out of the room answering a page, Alex unwittingly spilled the beans. The astute HMSers became suspicious when he said his six-year-old dog was older than he was. They solved the case when he told them his mother was outside, talking on the phone. When I returned, they reciprocated by describing an exam filled with horrendous neurological findings and an enlarged spleen.

At the end of the lunchless day, there is no need to pack my briefcase, as it is already full of the reviews, journals, and manuscripts I have been carrying back and forth for the past two weeks. Fighting to get out of the garage where I am boxed in by seven cars, I manage to pick up Alex at his after-school program only five minutes late ($5 fine). The ride home is unilluminating. Apparently, aside from the brush with electrocution, nothing else happened at school. This is all part of a conspiracy by second-graders to keep their parents entirely in the dark. When we get home, he goes off to practice his piano and do his homework alone (he's learned that advice from his mother usually gets him into trouble with his teacher). I rush to the kitchen to find I forgot to defrost anything this morning (or maybe the dog ate it). Fortunately we have a programmable phone that has the local pizza place on a direct line. With the dinner boxes cleared away, I settle down with the *Times* for a few minutes while Alex watches Danger Mouse. At eight o'clock, he comes to get me to put him to bed, but once again he ends up folding my paper, tucking the afghan around me, turning off the light, and tiptoeing out of the room.

When I was asked to write this article, I explained that there were more appropriate C/S/Ms to approach. I was shocked to hear that they were the ones who suggested me! Perhaps our impressions of one another are not accurate. In fact, the really successful C/S/M may not exist. One thing I am sure of, however, is that at least one wonderful C/S/F exists. Ask Alex about him. □

Orah Platt '73 is assistant professor of pediatrics. Her research is in red blood cell membrane potentials. Last year she received an HMS Prize for Excellence in Teaching.

Changing Male Expectations

by Judith Herzfeld

DURING MY DECADE ON THE HARVARD faculty, I have participated in Ph.D. thesis examinations of several very capable young women. Recently I have taken particular pleasure in these occasions because these students have exuded a sense of belonging and a degree of confidence that I think were unknown among my contemporaries.

In my own case, I had come from as positive an early background as one could imagine. As a product of post-Sputnik secondary programs that cultivated scientific talent wherever it could be found, and an elite women's college with a large proportion of female faculty, I attained my baccalaureate with the expectation that I could, should, and would be a research scientist if only I wanted to be.

I soon discovered that outside the environments in which I had been nurtured, there were many esteemed scientists who doubted the "could, should, and would" I took for granted. In any given instance it was difficult to know how much these doubts had to do with me personally, and how much with my sex. I gradually realized that the latter was generally not to be discounted.

The first plainly spoken doubt came from a Nobel laureate at the university with which my college was affiliated. Having earned a top grade in his course, I was interested in his opinion of which graduate school I should choose. Looking out the window of his office, he would only say, "It doesn't matter." Rather puzzled, I assumed he meant the schools were all among the best. I soon learned from others who knew him better that he meant a woman wouldn't make use of graduate training anyway. In fact, it was not uncommon at that time for faculty to feel that graduate slots should be given preferentially to men because they would make better use of the education.

Others had different concerns. In graduate school, my class was one of the first in which women were allowed real teaching assistantships. Earlier women in the department had been allowed only to grade papers—on the grounds that they might become upset in the classroom if they could not answer the questions of aggressive male undergraduates. I was to find that the male undergraduates were generally more comfortable and sensible with female instructors than were the male graduate students with female peers or the male faculty with female protégées.

Some years later, with my Ph.D. and one year as an assistant professor at an elite men's college behind me, I married a fellow scientist. After shaking hands all around at the wedding reception, another prize-winning professor told us in his blunt way, "It'll never work, you know. There

are too many built-in conflicts." Rather stunned, we did our best to pretend he was joking. On our 10th anniversary we sent him a card commemorating the remark he no longer remembered having made.

These old stories are not worth remembering except to appreciate how much times have changed. I don't think my young counterpart today is likely to be told that it doesn't matter where she goes to graduate school or that her marriage won't work—partially because of a general consciousness-raising that has resulted from the women's movement, but also because her professors generally have had different experiences than mine.

The story has it that my Nobel laureate professor had a bright daughter who had gone to graduate school but had then given up her career to devote her energies more fully to her family. Our wedding guest, on the other hand, had spoken out of the pain of his own recent divorce. His wife had left him and two growing children for another relationship that made fewer demands on her career. In a sense, she could have been the daughter of my Nobel laureate except that she gave up the marriage instead of the career. Neither of these men had a low opinion of the intelligence of women and both wanted the women they loved to be their intellectual equals. But they had underestimated the all-or-none fashion in which traditional expectations forced such women to choose between family and career.

Of course, even without the burden of such expectations, there are some built-in conflicts. With only 24 hours in the day, I am very aware that my science would be different if I did not have children—not necessarily better, but surely more prolific. And my parenting would be different if I did not have a career—again, not necessarily better, but undoubtedly more completely involved. In either instance my life would be far less rich, and I would bring a narrower perspective to my roles as scientist, parent, and spouse. My husband faces similar trade-offs; to the extent that we share the burden of career-family conflicts, we avoid the resentments that can destroy a marriage.

Primarily because more and more members of our faculty are living within these parameters, my young counterpart is guided with more sympathetic expectations than I was. Her professor might be one I know who happily brags about baby-sitting for his grandchildren on weekends when his daughter and son-in-law are both on call, or another who takes pride in dressing and feeding his children in the morning so his wife can get an early start at work. These people won't tell her it is easy, but they also won't discourage or discount her. Of course, there are still unreconstructed professors around. But there are also growing numbers of women on graduate faculties who can help students dispel doubts and reaffirm dreams. □

Judith Herzfeld is associate professor of physiology and biophysics. Her research concerns both statistical mechanical studies of the effect of molecular packing constraints on the properties of polymerizing proteins, and solid-state nuclear magnetic resonance studies of bacteriorhodopsin, a light-driven proton pump. Author of Sense and Sensibility in Childbirth: A Guide to Supportive Obstetrical Care, *she is the mother of two girls, ages three and seven.*

Test Tubes and Babies

by Story C. Landis

I CAN'T REMEMBER MAKING A DECISION to have a family. In retrospect, it seems to have been an assumption on my part, derived from my middle-class suburban background as well as from my parents, that I would eventually marry and have children. During graduate school I married Dennis Landis, then a medical student, now a neurologist/neurobiologist at Massachusetts General Hospital. In contrast, it was certainly not assumed that I would have a career. My interest in science came from a high school teacher, good biology courses at college, and a senior thesis project that yielded unexpected results. My college was a women's school with many women professors who served as role models; it never occurred to me that I couldn't be a professor and have my own lab.

The decision, then, was not *whether* to have a child, but *when*. Two variables factored into this question for me, as they seem to for most women. First, there is no convenient time. Second, the biological clock is ticking away. Some women I know, like me, become pregnant when anxiety about the clock overwhelms anxiety about the profession.

Some of us deal more rationally than others with our ambivalence about the changes in lifestyle a baby requires. A pregnant clinical acquaintance of mine denied the coming changes by neglecting to obtain patient coverage for the month following delivery. In my case, I went ahead and submitted an abstract to the annual Neurosciences meeting, held that year in Los Angeles. I had requested and was assigned a poster presentation, in front of which I stood at the meeting for three hours as my ankles swelled ever larger. Since I was eight months pregnant and gargantuan, I could easily have doubled the poster area by hanging posterboards fore and aft. I worked until the day I delivered; when I couldn't work effectively in the lab because my belly kept bumping the fine advance on the microtome and I couldn't get close enough to the dissecting scope to see through the binoculars, I finished a manuscript, which was mailed off just before Michael was born.

The biology of parenting was the easy part. Pregnancy and delivery were inexorable once initiated. Integrating my work, Dennis's work, and care of Michael was, and remains, more complicated. Michael was the first baby born to a professional woman in the Neurobiology Department. I was an instructor at the time and felt rather like a test case. It seemed important to ensure that Michael's birth didn't change my identity too drastically; becoming a mother didn't

preclude being a scientist. As a consequence, when Michael was two weeks old, he and I went to the lab together for the first time. We continued to do so most days for about 10 weeks. We went to lunch seminars and lab meetings; I worked half-time at mothering and half-time at experimenting. Such an arrangement required a tolerant and supportive department, a private office, and a great deal of patience on my part and Michael's.

Since then, five babies have been born to women who were post-docs or instructors in the Neurobiology Department. None of those babies were brought in. Instead, their mothers took four- to six-week leaves of absence before returning without the baby.

Most young women are curious about the combination of science and children, since they envision this dualism in their future. However, a few of my younger female colleagues writhe at the public mention of Pampers, the tooth fairy, or chicken pox. To them, children are incompatible with a professional demeanor. They seem to feel that for me to discuss my child compromises my professionalism, which in turn compromises theirs. Children, like dirty laundry, are not to be aired in public. One wonders about the source of this attitude. Perhaps it has been acquired from more senior colleagues, male and female, who question the professional commitment to science of a woman who chooses to have children. When I was pregnant and looking for a position, one chairman asked whether I wouldn't prefer to work as a research associate supported on someone else's grant because a "real job" meant getting my own grant and teaching. I wouldn't argue that children aren't a distraction, because Michael is. However, he is probably no more demanding than a serious avocation (to music, for example), and certainly as rewarding.

Seven years ago, I calculated that there were 70 day-care slots for infants in the entire greater Boston area. By chance, when he was nine months old, Michael (who had been staying during the day with someone who had a baby almost his age) got one of those precious slots at a center in Newton, midway between work and home and maximally inconvenient for visits to the pediatrician. Now, of course, there are many more babies born to professional women, consciousness has been raised, and so there are several centers within walking distance of HMS. Even so, inevitably there are times when alternative child care must be arranged, and parents frantically patch something together.

One advantage of a formal day-care center is that it doesn't get sick, as a sitter can. However, if your child gets sick—and children in day care catch anything and everything in the Boston germ pool (and then pass it on to their parents)—he or she can't go. Even this disadvantage has its good side: in contrast to most kids, the day-care center graduate will have weathered all the illnesses by kindergarten, and will have a perfect attendance record in primary school.

The decision was not whether to have a child, but when. Two variables factored into this question: there is no convenient time, and the biological clock is ticking away.

Some aspects of child care become easier as the child gets older: for example, on the weekends Michael—now a cheerful and self-sufficient first-grader—often chooses to play with the neighbors' son, so we are free to catch up on our work. Other aspects become more difficult: for instance, there is a year-long waiting list for after-school care in our community. Trustworthy and likeable people willing to work part-time are difficult to find and harder to keep. We have bribed our present sitter with the use of my car during the week.

The crux of the issue in managing a child and a profession is time. There is never enough. The child becomes a magnet—instead of spending extra hours in the lab, one wants to be at home. When Michael began to go to the Children's Center, Dennis and I began "tag-team parenting." One of us would drop him off at 8 am, the other would pick him up before 6 pm (centers and even sitters have regular hours, and they fine you if you are late). If I picked up, I could go into work as early as I could get up. If I dropped off in the morning, I could stay at work as late as I wanted. Sometimes days would go by before Michael would see both of us at once. Even so, time to fill professional demands was finite. When it was time to pick up, I had to go whether the experiment was done or not. Fortunately, my research tools, largely anatomical, are reasonably compatible with these constraints.

For me, the most significant change has been the loss of casual conversation over lunch or in the hall that often leads to fruitful collaborations. Even now, I become uncomfortable if I spend more than five minutes talking about something nonprofessional at work. One becomes incredibly efficient because one can't retrieve the lost time by staying late. Dennis suffers the same time constraints; we share the burdens as well as the pleasures of parenting. In his case, the burdens weigh more heavily, since he has clinical responsibilities as well as research.

A corollary of the time problem is that there is no way everything can get done. One comes to accept slop in those areas where it doesn't really count, although I much prefer to think of this attitude as being flexible. I haven't seen the top of my desk in the lab for a month, Michael's dog hasn't had her distemper booster shot yet this year, and our house has cobwebs in every corner—but I just sent a manuscript to *Developmental Biology*, my grant proposal was submitted on time, and I have been to all the Little League games so far this spring. A partial solution is to relinquish the egalitarian attitudes of the 1960s and pay someone else to do the things one doesn't have the time or inclination to do, such as laundry and bathrooms.

Of the scientific mothers I know, not one seems to regret the decision to have children. We all try to make the task of balancing responsibilities seem as effortless as possible; the accomplishments of each of us seem commensurate with what we would have achieved without the additional challenge. However, it's clearly not a controlled experiment. □

Story C. Landis, Ph.D., is associate professor of neurobiology. Her primary research interest is developmental neurobiology, studying how functionally appropriate synaptic connections are made between neurons and their targets.

Role Modeling for Medical Students...

by Kathryn Beck Kris

When Julius Silberger And I Became the two new psychiatrists at Harvard Medical Area Health Service in 1980, I discovered that I had become a role model for women medical students. In the Class of 1984, 61 percent of the women consulted with the University Mental Health Services sometime during their four years, usually for transient developmental problems. Only 25 percent of the men did so. When given a choice, over 85 percent of the women (and 74 percent of the men) selected the psychiatrist of their own gender.

When I asked the women students why they selected me, they told me it was because I was a woman. Some did not believe a man could understand them. Others sought the special understanding of a woman who had been through similar medical school experiences. Most frequently, they hoped I could understand the strain they experienced combining medicine with hopes for marriage and children. Although fearful of intruding, they wanted to know whether I had enjoyed marriage, children, and my medical career, and they were relieved that I had not had to sacrifice one completely for the other. To my surprise, still others wanted to support me and make me a success, as they hoped other women would do for them! Some said they were looking for the comfort they had felt in talking about emotions with their mothers, but not their fathers. They sought reassurance that they could maintain acceptance of themselves, derived from an identification with their mothers, in the primarily male world of medicine. Yet when I asked them if they sought me out as a role model, they objected to the idea that they were imitating or modeling themselves after anyone.

I learned that women medical students are looking not only for a successful career woman with whom to identify, but for a woman physician who combines a successful medical career with a variety of other interests, most commonly marriage and children. At every major transition in medical school—the initial adjustment to new work and friends, Introduction to Clinical Medicine, and the last year, with its loss of relationships and anticipation of internship—they seek reassurance that they will be able to achieve their own career and personal goals.

In ICM, some fear that sensitivity to patients' feelings must be sacrificed for the initiative required by the physical examination, or by the competition of formal presentation. To my surprise, some of the most successful women become acutely depressed when they learn of their acceptance to the leading internships, because they fear their career success will preclude satisfying future relationships. Unmarried women may not be able to maintain their optimism that both career and marriage are possible. Boyfriends or husbands who are strained by their girlfriends' or wives' approaching internship sometimes aggravate women's fear.

In response to these developmental worries, for the past two years Carola Eisenberg, dean of student affairs; Arthur Kravitz, assistant clinical professor of psychiatry; George Fishman, instructor in psychiatry; and I have chaired oversubscribed and emotionally moving workshops in which residents and junior faculty discuss with students how they have managed the relationship side of their lives during the demanding early years of post-graduate medicine.

I recall my own feelings on entering HMS 30 years ago. I panicked in the month before matriculating; I told my parents I wasn't sure I could do it. I knew of my father's admiration for his women classmates from Johns Hopkins Medical School, but I was troubled that they weren't married. I feared I was entering a nunnery (in a class of seven women and 125 men!), and that spinsterhood was inevitable. My father's saying "the soup isn't eaten as hot as it's cooked" somehow reassured me, although it has taken me close to 30 years to understand what he meant.

In the preclinical years, Harriet Hardy in toxicology and Helen Padycula in histology were my only women teachers. I was glad they were there, but I saw them too rarely to feel a kinship with them. In the clinical years I knew of Marian Ropes, Helen Pitman, Anne Forbes, and Janet McArthur, but I never saw them in action. I remember that Robert Gross invited Helen Taussig to lecture to our third-year class on the Blue Baby Operation, which she and Alfred Blalock had devised. It was important to me that her contribution was recognized nationally and at my school.

Psychiatry at Beth Israel Hospital was the striking exception to my expectation that women in medicine were deferential—at most the power behind the throne. Grete Bibring's effect on medical student teaching—directly in lectures and indirectly in clinical rotations and in her influence on Herrman Blumgart and other department chairmen—pervaded the whole hospital. Although my interest in psychiatry began in college with Freud's writings, Lydia Dawes, Helen Tartakoff, and Malvina Stock, all at BIH, and other prominent women psychiatrists in the larger Boston psychiatric community, enabled me to feel that a woman could be at home in the field at almost any level. □

Kathryn Beck Kris '59 is psychiatrist at Harvard University Health Service, Medical Area, and chair of the subcommittee on research of the Joint Committee on the Status of Women. Her research interests are medical students and impaired physicians. She recently published "Developmental Strains of Women Medical Students" in the Journal of the American Women's Association, *September-October 1985.*

...And for Graduate Students

by Joanne S. Ingwall

GRADUATE STUDENTS IN MEDICAL schools are often an invisible group. The more than 70 female graduate students (Ph.D. or M.D./Ph.D. candidates) at HMS are scattered throughout the campuses on both sides of the river, and rarely have a chance to meet one another. Given the low percentages of women faculty in the preclinical and basic science departments, they also have little opportunity to observe role models or develop mentor relationships with women. From observing my colleagues over the past 25 years I have learned that most women find it difficult, though certainly not impossible, to establish mentor relationships with men.

When I was a graduate student at Cornell University 20 years ago, there were no female faculty members—indeed, only in the past few years have the chemistry departments at schools such as Cornell and Stanford hired women junior faculty. Out of our class of 30 graduate students, there were five women, an unusually large number. Three of us completed our Ph.D.s; one left with an M.S., choosing to follow her spouse, and another left with no degree.

At that time, a woman's place in the laboratory combined traditional female roles with serious science. I was the unofficial hostess, helping foreign students and fellows with housing, and organizing the annual picnic as well as the freezer cleanouts. Following my thesis defense, I thanked my adviser, a prominent physical chemist who was then chairman of the department, for having me as his student. He replied that he had taken me on as an "extra" student; I had not "taken a man's place." This from a wonderful man whose wife had a career and whose two daughters went on to become successful professionals!

The number of female role models and mentors did not improve during my post-doctoral and junior faculty years. I did begin to interact with senior women, but they were not role models. Often I perceived them as less than fully committed to research, and therefore not to be emulated. Some were simply not likeable. Never did any offer counsel on how to plan a career. Happily for me, several male senior faculty members have been helpful as mentors.

As chair of the medical area Joint Committee on the Status of Women, I have become sensitive to the problems of promotion and retention of women faculty at HMS. Junior faculty need to learn what is really required for promotion, how to develop a scientific reputation, and how to weigh the pluses and minuses of teaching and committee service.

JCSW has organized discussions for newly appointed women assistant professors to tell them, "Now is the time to begin working on the next hurdle, promotion to associate professor, and this is how to do it." At one of the most outstanding of these sessions a few years ago, it was amazing to see the lights go on for these new appointees as Mary Ellen Avery, then physician-in-chief, Department of Pediatrics at Children's Hospital, advised them to take time out to rejuvenate mind and body, admonished women for not asking for raises, and gave advice on how to package successful research projects.

Serving as a mentor is not always easy. At a recent luncheon I chaired for women M.D./ Ph.D. students, almost the entire two-hour period was devoted to the subject of integrating parenting and career: Is it best to have children before or after postdoctoral training? How much will my all-male colleagues hassle me if I get pregnant? What are the responsibilities of the student and hospital staff in dealing with pregnancy during residency? How can a woman junior faculty member take time off to deliver her child and still satisfy her responsibilities as a member of a busy medical team? How does one balance family demands with traveling to meetings? Answering these questions was no small feat for me, as I have no children; JCSW will sponsor a parenting conference in October to address these issues.

In the past, many senior women felt that they expended all their energy on career and family and had no time or energy left over for mentoring. Others saw junior women researchers as competing with them for the one "token woman" position. As I heard from colleagues, the late Leah Lowenstein, who was professor of medicine at Boston University and then in 1982 became dean of Jefferson Medical College (she was the only active woman dean of a major American medical school at that time), proved that one could be both successful and generous. She often organized evenings at her home for women student-faculty discussions, giving advice on careers and assuring women that it is all right to pay someone to do one's housekeeping, teaching by example how to be both role model and mentor.

The 10 women full professors and 41 associate professors at HMS this academic year serve as role models, whether they are aware of it or not. They face the challenge of being visible to the medical school community and being generous with counsel while still maintaining productive scientific careers. Some find this challenge burdensome, but being responsible women professionals means responding to the needs of women students and faculty who are developing careers in academic medicine. Both women and the school will benefit. □

Joanne S. Ingwall, Ph.D., is associate professor of physiology and biophysics in the Department of Medicine and director of the Nuclear Magnetic Resonance Laboratory. Her primary research interest is regulation of energy metabolism in developing and adult cardiac muscle.

Meeting THE PRESS

A Round Table on Science and Journalism

How can scientists and journalists most effectively deal with one another? What motivations do the two camps bring to their interactions? Is there distortion in science reporting? If so, what causes it, and how can it be lessened?

To answer these questions and others—for the scientist, whose work is reported in the press, and the physician, whose patients are influenced and informed by that reporting—the Bulletin *held a round-table discussion in April among six participants in the science-journalism relationship. Managing editor Lisa W. Drew was moderator.*

Richard Knox is a science and medicine reporter for The Boston Globe. *Philip Hilts is a science and medicine reporter for* The Washington Post, *and author of* Scientific Temperaments: Three Lives in Contemporary Science. *He was at Harvard this past year as a Nieman Fellow. William Haseltine is HMS associate professor of pathology at Dana Farber Cancer Institute, and HSPH professor of microbiology. As his research involves the disturbing, and much reported upon, disease AIDS (acquired immune deficiency syndrome), he has experience with the press. Arnold Relman is editor of* The New England Journal of Medicine. *Elissa Ely is an HMS student ('87) with a science writing background.*

Jay Winsten is HSPH assistant dean for public and community affairs, and will be director of the new HSPH Center for Health Communication. Over the past three years, he has interviewed 27 science reporters and editors in an extensive study of the forces in science journalism. The spring Health Affairs *carries an article by Winsten on the subject. He plans to develop a second project to advise scientists how to deal with press.*

Drew: Jay Winsten will start off the discussion with an example of a science news story that raises some fundamental questions.

Winsten: The *Bulletin* asked me to think about a case that could help frame some of the issues. *The New England Journal of Medicine* once published a study that found a statistical association between coffee consumption and pancreatic cancer. The scientist's institution did not call a press conference, or issue a press release.

When reporters called the scientist—not unexpectedly, given the potent combination of the general public's coffee consumption habits and fear of cancer—he was willing to be interviewed. Reporters pressed him to offer a public policy recommendation. He resisted answering. He said it was a complete study, but it would have to be replicated by others before we would know whether the finding would hold up.

At least two reporters pressed further, asking, "Have you changed your habits as a result of the study?" He said, "Yes, I've stopped drinking coffee." Those reporters were convinced by his answer that he believed the findings—and that his public posture was that of a cautious scientist.

His response strengthened enormously the news stories that resulted. Subsequently, parenthetically, other studies have not confirmed that same finding—and have not been extensively publicized.

This case raises several questions. Was the question about the researcher's personal attitudes appropriate? Did the researcher have a public responsibility to respond? He could, after all, have said something like, "It is a preliminary finding that does not justify, at this point, a policy recommendation. Your question is an attempt to draw me into an implicit recommendation that would be inappropriate." How should a reporter handle the response that the scientist did give in order to put the overall report in context?

Hilts: *The Washington Post* did follow up on the issue. In covering a later study, we explored various problems caused by coffee—saying, essentially, that it didn't seem to cause what it seemed to have caused before.

Winsten: My impression is that the most widely disseminated story was the initial one, and that there wasn't anything like that kind of blanket coverage for any follow-ups.

Knox: There have been follow-up stories over the years covering published studies that didn't replicate the original finding. I know *The Boston Globe* had some.

The nature of science, and certainly of science reporting, is that no one study is going to tell the story. One tries one's best to put it in context at the time. Probably a journalist would be more inclined to err in overestimating the importance of a given finding. But what harm was done in presenting that study in a slightly over-inflated way? Some people might have changed their coffee habits, and later may have been reassured to hear they didn't have to.

Winsten: The cumulative harm is substantial, because over a period of time the public concludes, "Everything causes cancer."

Knox: We are getting better at that. I can recall the cyclamate stories 10 or 15 years ago pretty vividly. There was a lot less context, balance, and caution in reporting about cancer-causing agents than there is today.

Hilts: Scientists have changed, too, in their attitudes toward what causes cancer and what that means for public policy. They were quite alarmist a few years back.

Haseltine: I agree. People were enthusiastic about being able to trace the causes of cancer in various foodstuffs, and there was a big push for research on prevention. Any scientist who finds something new is going to be enthusiastic about it. After all, he or she spent 20 to 30 years getting to that point. Many scientific communities were brought up short with the realization that 90 percent of mutagens aren't carcinogens.

Ely: One of the pressures on the press is not simply to report the news but to translate it. I think the question about drinking coffee was valid and legitimate. The responsibility of a science writer is not simply to describe, but to make a relevant connection. Most of the readers may not have read the rest of the article; I guess that is the problem.

Winsten: I think that if the scientist can see his way clear to a policy recommendation, he does have a public responsibility to put it forward.

Philip Hilts, The Washington Post

Haseltine: We are facing an issue much more serious than coffee drinking, which is the AIDS problem. I can imagine a reporter asking an AIDS researcher, "If you were diagnosed as having AIDS, would you leave your family because of the risk of giving it to your children?"

Winsten: And another major question, on an issue we'll have to face soon: "Do you think we should set up social systems equivalent to leper colonies as a result of the possibility of uncontrolled contagion?" You are going to get a variety of answers, based on the

PHOTOS BY JERRY BERNDT

scientists' personal opinions, political stances, and visions of themselves in society. It is going to be the responsibility of the press to interpret a wide spectrum of answers. Because there is going to be a tremendous panic.

Knox: Interpreting this evolving problem is going to be one of the biggest challenges science writers and medical writers have faced. We are going to be living with uncertainty for a long, long time.

Haseltine: I've had more exposure to the press this last year than ever before, and I think most scientists don't understand, right away, the pressure on reporters for news. What appears to be news is sometimes not necessarily built on facts, or the way scientists think, but on the controversies—both personal and scientific. If I remember the coffee story, there were stories having to do with controversial interpretations.

Drew: Let's go back to the question "Have you changed your habits as a result of this study?" That reporter must have been delighted to come up with that question. What goes through the reporter's mind?

Knox: In asking that kind of a question, you can be trying to get beyond the scientist's reluctance to not only talk about the implications at all, but just to talk about the facts. That is not sneaky. It is not an attempt to trick the scientist into saying something he or she doesn't want to say. Hopefully you are dealing with a scientist—not always the case—who knows what he or she wants and doesn't want to say. Optimally, you would also like to talk to other scientists in the field. You might get some opposing views. And you might say, when I say that, "Controversy! That is what journalists like."

Well, it's true, but often controversy is a signpost to some of the more important dimensions of the study. If you can only find the people to talk about it openly, you get a feel for what the controversy is about, how sound the study is.

Hilts: If you had a researcher friend who had just done a big study, and he said over lunch, "Listen, I am going to stop drinking coffee because of my study," you might also want to stop. There is no reason for a reporter not to ask for that, and pass it on—again, with other information about how preliminary the results are.

Ely: Dick used a good word, which was "dimension." As a science writer, you are the door between separate and discordant dimensions: between scientists and scientists, and scientists and laymen, with their separate agendas. You are almost the doorstop.

Knox: Having been to a lot of press conferences, I realize that a question like that, or much more outrageous questions, can elicit answers from the startled researchers that can be misinterpreted. The wrong lesson to be drawn is that certain things shouldn't be asked. I probably don't ask as many outrageous questions as I should. I probably wouldn't ask if we should treat AIDS patients as lepers, or if we should follow with computers people who are antibody positive. Someone else might ask those questions and elicit interesting and thoughtful answers.

Ely: Maybe part of what you need to do, then, is explain to your readers why those questions aren't outrageous.

Knox: We ought to acknowledge here that much of what journalists do is react. There is an active aspect, as there should be, that takes the form of interpretation. But I am not telling the reader what I think of this guy's or that team's work. I am trying to gather, collate, interpret, get people to react against one another—and hopefully develop a context for that work to be seen in.

Relman: That is a valid statement for a reporter with professional integrity, such as you, but not an accurate description of how your craft behaves in general. Many science stories represent a choice as to what kind of coverage, how much play, how much publicity, a given event is going to receive. I am thinking, for example, about the artificial heart story. That was a medical event: a quasi-scientific, quasi-research event. But it was dealt with. Many responsible reporters reported it as if it were an important scientific development. The play given a story like that clearly represents the choice of the media, stimulated by the source of the information.

Jay Winsten, Ph.D., Harvard School of Public Health

Hilts: Well, it started out with the choice of Humana Hospital to do a bizarre series of things like that.

Relman: Right, and to act/play it up.

Hilts: Large figures in the field choosing to do that and stand out in front—again, as Dick was saying, this is reactive. And when there is a question of interpretation, as with Humana, what do you do? You don't decide for yourself what the policy is. You have to go around asking.

Relman: It was clear that the medical profession was in no way prepared to say how important the implantation of the artificial heart was going to be. It raised all kinds of interesting questions. But few people of repute in the field were prepared to say that this was a significant step.

Hilts: I'm wondering what you think about that coverage.

Relman: I think it was bizarre. I think it was excessive, erratic, idiosyncratic. Now, when the most important things have been happening, that the public really ought to know about, there is no coverage. Of course, that is in part due to the fact that the company and the doctor involved, DeVries, have backed away. They don't hold press conferences. Nevertheless, if reporters wanted to keep the public informed about what is really happening, they could do so.

Knox: Well, we shall do that—but there is a fallacy implicit in some of what you say, which is that something has to be scientifically significant, perhaps valid, in order to properly cross the threshold of news. That isn't true at all. There is much in the world of science and medicine that we know will not turn out to be sound or significant, but that is certainly part of the landscape. We are trying to describe that landscape and all its occasional bizarreness and controversy.

You also talk about the media choosing. I hope one of the take-home points of this discussion will be that the media ain't no monolith. Yes, the media did focus an enormous amount of attention on the artificial heart, but what really is the acceptable alternative? It certainly isn't to let DeVries and Humana do a series of seven patients, wait two years until a case review is published, and then report on what Humana has been up to.

Hilts: If we are going to talk about good journalists and good scientists, we shouldn't talk about crummy journalists and good scientists. Let's not mix them up. If we're talking about lousy media coverage, let's talk about lousy scientists.

Drew: In what ways do scientists manipulate the press?

Hilts: There are a lot of things that scientists do that are not so great. It's a profession like anything else, like journalism, like law: you have people who are less smart and less ethical. Press conferences are called when they have no business being called. Studies known to be weak are pushed as strong. Lies—that happens.

Knox: Manipulate is a loaded word. We were talking earlier about the pressures on news people. There also are pressures on scientists. If they believe in the work, they often want it to be noticed. The institutions in which they work have a strong interest in getting the word out about what their people are doing—which feeds back on the chances of getting funding. We are part of that dynamic—sometimes an uncomfortable part—and we have to be alert to it.

I remember going to a press conference held by a Boston hospital about two years ago, at which I asked (I guess I got out of the wrong side of the bed that morning), "Why are you having this press conference?"

From the laughter that ensued, I think it had become increasingly obvious to everybody in the room that this was a press conference in search of a news story. They haven't called those kinds of conferences recently.

Relman: The issues that deal with public policy and the public interest—ethical, legal, economic issues—are all appropriate grist for the science writer's mill. But let's look at how the writer chooses to present the story. It's not at all clear, from the flow of events in biomedicine, what ought to be on page one. Most of the time it's a matter of editorial choice. My point simply is that the media often make the message. How the media choose to react determines whether or not a given subject is in the public eye.

I find inexplicable at times the way an important issue disappears without a ripple. You say, "What's happened? Have all the scientists stopped working on this problem? I missed the solution somehow." But you know what's happened: it isn't news anymore. The media ought to acknowledge that, and ought not to act as if they're simply reacting to objective phenomena, and that they're driven by events. They're *not* driven by the events.

Hilts: Stories do drop out, but I don't see why that's a problem. Our society isn't built only on newspapers. There are news magazines, then magazines with longer pieces, and then books, and that's where you'd expect the thing to go after it comes off the front page. Two years later, when we get another conclusion, it will come up in the papers, and then go down, and then come up. You can't expect the newspaper to carry the burden.

Relman: I would merely point out that your colleagues often argue their right to immediate publication of news on the basis of that function which now you deny.

Hilts: No, I was saying we have the function to do it now; we don't have the function to carry it on forever.

Relman: Except that often newspaper reporters, when they take their jobs seriously, will say, "we have an obligation to keep the public informed." I say, if you have that obligation, then by golly you ought to stick to your knitting, and they don't.

Knox: It's a flaw of both print and broadcast journalism that we don't follow through. But sometimes when a story drops out of sight for a while, it fits the pace of science and medical research itself—because, as you know, and often have said, things don't always happen in dramatic, nicely packaged increments. Science is a

Elissa Ely (HMS '87), science writer

subtle, fits-and-starts process.

Winsten: There is a natural dynamic to the news separate from the dynamic of science that progresses over time. Let's take the example of EDB, which surfaced in newspapers for the first time in a major way in December of '83, and then was a page-one story through March. The early stories were extremely inflammatory, provoked real hysteria, on the part of, primarily, housewives making muffins with EDB and serving them at breakfast.

It wasn't until February that, for the first time, a leading newspaper published a page-one article reporting a second school of thought about the extent of the risk. I asked the reporter, "Why is it that it takes over two months for the balance to make its way into a story that's breaking over time? Is it that you're playing catch-up—that it takes that long to develop contacts and to discover the other perspective?"

"Maybe that's part of it," he said. "Frankly, the more important reason is that after 10 weeks you need a new angle."

The public policy outcome was, I would suggest, significantly influenced by the fact that that second school of thought didn't surface in the public print until decisions at the federal level had already been made.

Drew: Is there a lesson for scientists in all this?

Knox: Often the scientists following those stories know full well the dimensions of the story that are not reaching the public. Hopefully, as a reporter, you have some contacts with those people, and somewhere along the line they say to you, "Look, this isn't all one-sided. There's a whole school of thought here."

One lesson for the scientist is that if you have built up a relationship of some trust with a journalist who's covering a story on an ongoing basis, you can confide in that reporter information that you don't want to be directly quoted on, for the benefit of his or her understanding. That can be abused: many scientists will try to put everything off the record, and some will try to do it retrospectively. You just can't do that. But you do feel your way, just as with any human relationship.

I was irritated some time ago when Dr. Relman published a commentary by a well-respected public-relations person who seemed to be counseling scientists to be wary of the media and of the tricks that would be played by a reporter given half a chance. That message doesn't further the cause of better science reporting. The only way you can get better science reporting is if scientists and journalists can talk to one another about complicated things.

Arnold Relman, M.D., The New England Journal of Medicine

Relman: It's natural that there should be difficulty in the interaction between scientists and reporters. Scientists deal with the press with many possible objectives, ranging from the most selfish—personal aggrandizement and economic motivation—to lofty ideas of trying to teach the public something. Reporters, too, come with varied motives—from personal ones ("I've got to get a scoop, get my story on the front page") to committed, professional ideas, again about educating the public.

Knox: Let it be said that Elissa and Phil and I love to get on the front page, or the equivalent if you're writing a magazine article, with a good story. You want to get people's attention and you want to make an impression.

Relman: That's what you're made for. But what are you prepared to do? How much are you prepared to compromise your values and your standards to get on the front page?

Knox: We're talking here about science writers, primarily, rather than the media in general. We're trying to figure out ways of illuminating how readers of the *Harvard Medical Alumni Bulletin* should interact with science writers. If you want to have any longevity as a science writer, you probably should worry about your credibility with the scientific community, because if you don't have it, you won't get many interviews, you won't build up contacts, people won't call you back. That is a real force, as real as the pressures to get on page one, or your three minutes on the network news.

Hilts: The overriding consideration, beyond anything else, when you're sitting down to write a news story, is that one mistake is enough to blow your career away. So you're not wondering how you can compromise yourself to get on the front page. That is very dangerous stuff. I guess I don't like to think of myself compromising my values. Do you think that really is something that journalists do?

Relman: Well, I raised the question of what you're prepared to do to get on the front page. I was not thinking primarily of something that would destroy you when revealed. I was thinking of things that color one's judgment, that change it from critical and conservative—in the good sense of the word—to not so prudent: going with the herd, going with the flow.

Winsten: In the interviews I've conducted with reporters, some have acknowledged being under pressure to, as one put it, "push at the boundaries of truth and accuracy to make

the strongest possible statement." Another talked about "pushing at the limits of the permissible." Every sentence is still going to be factually accurate.

Hilts: When you're writing a story, you're not thinking of how far you can push it alone. You're thinking about Arnold Relman in the back of your head. When he looks at this thing, is he going to say, "That's wrong," or is he going to say, "Yeah, that's about right"? You think about that when you're writing a sentence. You write it out; it looks too strong; you say, "That's really going too far. I'm not going to be able to back that up; I'm not going to feel good about that"—and you pull it back.

Winsten: We're not about to change the fundamental directions of two different professions. The drift of this discussion could lead to the conclusion that nothing can be done. But even within the set of pressures that both sets of players face, a substantial amount can still be done. One of the problems in medical news, for example, is that the reporter fails to describe and explain the obstacles to clinical application. It's not sufficient to simply state that more work will be done when it could take years.

Hilts: Who does that?

Winsten: Hardly any reporters actually describe and explain the obstacles.

Hilts: I don't buy that at all. That's not true.

Knox: Look, there's an amazing amount of stuff on medicine, every day, on the wires. I go through what I can at the end of the day on my computer terminal. I would not say that what I see on the wires usually fails to describe the appropriate caveats and limitations of what the scientists have done.

Winsten: Stories state that there are caveats, but they don't inform the reader what those caveats are. They don't help the reader understand why a result is still preliminary. In the case study of the coffee story, for example, I'd be surprised to go back and discover a story that describes how it could be that maybe these results will not be replicated with a change in setting.

Haseltine: I don't want to argue on the side of the reporter here, but what can you do? You can generally try to make people understand why science has its limitations. It's even hard for scientists to believe the limitations we have. It's hard to explain. Even to your colleagues.

Drew: How have you dealt with that when you've been approached by reporters?

Haseltine: I'll give you an example from what I'm working on now, which is AIDS vaccines. I say in answer to those questions, "Well, there's no way to predict where we are now and what will happen in the future. That doesn't mean we shouldn't work as hard as we can, and everybody's working hard."

Hilts: That one paragraph appears in an awful lot of stories.

Winsten: Let me give you an example. The New York State Department of Health called a press conference to announce a breakthrough in the application of vaccinia virus to be used in the development of a set of vaccines against a set of diseases. *The New York Times* ran a page-one story reporting that press conference. It was a single-source story. There was no one quoted who was not at that massive press conference. There wasn't one sentence that hinted at the fact that vaccine research in animals doesn't necessarily lead to an effective human vaccine. There was no description of the obstacles that arise in going from animal systems to the human. It was given as a flat statement that we're likely to have 10 different vaccines against 10 different diseases.

Knox: Well, that was a rather remarkable instance in which the press was manipulated.

Winsten: That's very common.

Knox: I wasn't there, and I didn't report on it, but I know of that conference. It is no more valid an example to cite than the recent AIDS meeting in Atlanta. There were a number of papers on clinical progress, such as it was, and the few drugs being tried. The stories I saw did not over-promise, and certainly did dwell on the obstacles to successful treatment.

Ely: I have a question, as a neophyte. What is your sense of what your readers want?

Hilts: I'd like to say something about that, because it's a mistaken assumption that we write for readers. You're thinking about the story, the facts, the other paper, the pressures. The reader is assumed, always.

Haseltine: There are more audiences in a scientist's mind than may be in the reporter's mind. Certainly the scientist is speaking to his colleagues as clearly as he's speaking to anyone else. He's speaking to the people at the funding agencies; he's speaking to his congressman; he's speaking to the president of his institute.

Knox: The most satisfaction in being a journalist is when you can write a story that speaks at a number of different levels at once—when you can carry deeply into the story the person who is completely unsophisticated about science, as well as say something to which the scientists most

William Haseltine, Ph.D., HMS, HSPH, Dana Farber Cancer Institute

Richard Knox. The Boston Globe

intimately involved will react with, "Yeah, he got that right." And even, although this is rare, put it together in a way people in the field haven't thought of before.

Haseltine: That happens more and more now. I think of why I would put a reporter onto something. I might say to Harold Schmeck of *The New York Times*, "Listen, Harold, look at papillomavirus now, good area; here are five people to talk to." I would do that because there's a whole area—the importance of these viruses in human disease—that I think my colleagues should be aware of, as well as the public.

Relman: Despite my criticisms, I do believe science reporting in general is getting better. There are qualified reporters. More money is being spent. The market is bigger. But we're such a big country that even as things are getting better on one edge, they're getting worse at the other edge.

Drew: What recommendations do you have for the scientist that would help lead to that optimum story?

Haseltine: It's been helpful for me to be able to consult Jay and others. How do you know who the reporter is? A liaison person can tell you, "This guy's got a rotten record; this guy's got a good record. This kind of story might be important. You're really going to have a press conference, or not have a press conference." There should be liaison people in major universities.

Hilts: Like anything else, that can be misused, and some institutions try to overdo it. The best people in that business will probably spend a considerable fraction of their time trying to counsel their people not to say something, not to call a press conference at this juncture, because they're often very close to it, and they may not have the right perspective.

Drew: Let's talk about the one-to-one. Let's say you contact someone who doesn't have much experience with reporters. What advice can you offer that person?

Knox: It would be too much to expect that most scientists will have very many contacts with the press over their careers—unless you happen to be working in something like AIDS, which is hot. That goes back to relying on someone within your institution to counsel you. First, it's a good idea to let that person know when you've got a paper in press, when it's supposed to be out, and when you're going to be giving a presentation. Then that person has time to understand what it's about, work with you on it, and make sure it gets handled in a first-class way when the onslaught comes.

Second, you have to do some triaging of the reporters you talk to. It helps, when you expect a real onslaught of calls, to set aside the time. You just don't plan to do anything else. You make yourself available for a day or two days for interviews—which is a drag but might be worth the investment.

If your work is not quite so guaranteed to get a reaction, maybe you get a call out of the blue from the reporter. Then you have to fall back on your instincts, and try to gauge what kind of story that person's working on—and his or her experience and understanding. Try not to dodge and weave too much, and try not to decide for the reporter—if you feel you can trust him or her—what the public should know.

Hilts: That bit about dodging and weaving is critical. You have to be honest. It helps for reporters to know, "Okay, this is what I'm going to say, and there are some things I'm not going to say," and leave it at that—instead of trying to weasel around, because that makes a reporter think there's something else going on.

Haseltine: There's another constraint we've touched on briefly—and that is time. We don't have much, and there are a lot of reporters in the world. If you work in a field like AIDS, you're going to be besieged, and you've got to make some drastic choices.

Knox: How do you handle that?

Haseltine: I talk to four or five people. That's it, no more.

Relman: The first four who call?

Haseltine: No, I find out who are the most responsible reporters.

Drew: I have one more question. How do you decide what a story is? You pick up *The New England Journal*, or maybe Bill Haseltine calls you to say, "You might be interested in this area." How else do you do it?

Hilts: You decide what's news. You just have to decide. There are no rules.

Knox: One of my favorite metaphors is a cartoon that shows a grizzled and bent-over old man with a beard looking through a telescope at the heavens, peering in one direction. And his counselor, or wife, sees a comet over there and is wildly tapping him on the back, saying, "No, no, over there." That's often what it feels like, that you're looking in the wrong sector of the heavens. It's a capricious business.

Hilts: The surest definition I've ever heard is that news is true, remarkable stories. And I don't think you can say a whole lot more than that. You must have some reference for "true."

You must talk to Relman, you must think about your own experience, you must have read something. And then "remarkable": it's something that is not common, already there.

Relman: I would simply add, predictably, that to know whether something is likely to be true or not, you need available evidence. So I like to suggest that part of the definition of news and science involves the availability of evidence—without which many of the events that are treated as news in science may be questionable.

Knox: Two aspects of science should be reflected in the reporting: the evidence you speak of, and the process. Over time we ought to give the public a feel for the way science proceeds. There's too little appreciation for the accretion of information that makes something important.

The only way I can think of to counter that tendency is to give people a window on the process, the controversy, the uncertainty, the fact that you've got to make some important decisions on the basis of much less information than you'd like. And that, in turn, involves access to scientists at times when they might not find it most convenient to talk to you—times when, in their view, things are not ready to report. That's where a lot of our conflict comes in. We just have to feel our way, but I would like to make a plea that at least occasionally scientists will deal with reporters who seem to be interested in that kind of reporting. □

A Word from the Harvard Medical Area News Office

Below, Lillian Blacker, director of the Harvard Medical Area News Office, offers advice to scientists approached by the press. The News Office reports on research or clinical findings of HMS scientists in FOCUS, *a publication that comes out weekly during the academic year, and is sent to 7,800 readers, of whom about 200 are medical science reporters and free lancers around the country. The News Office staff is available to HMS scientists for advice and counsel in dealings with the press.*

The public appetite for medical and science news seems insatiable these days, and one of the happy consequences is the emergence of a cadre of well-informed medical and science reporters. To feed the public's hunger for health news, all the media—print, radio, and television—are in touch with the medical schools, hospitals, and individual scientists in search of the latest breakthrough, cure, or treatment.

A less cheerful outcome of the popularization of medical news is the competitive need of the media to cover events even if they are not fortunate enough to have a well-qualified reporter to do it.

Several Harvard-affiliated hospitals have guidelines that physicians and researchers may follow when a request comes from a journalist. The News Office has some additional suggestions. Ask yourself the following questions: Has the work under discussion been peer-reviewed for a publication or meeting, and will an interview jeopardize subsequent professional publication? Is it good for science if I agree to the interview? Is it useful for the public? Is it good for HMS? For my hospital? My center? Is it good for me? Is the material ripe for this kind of discussion, or is it premature? Are there colleagues who should participate or be named? Is the reporter knowledgeable, trustworthy, familiar? Is the publication or station or program an appropriate medium for telling the story? Should I be talking to one reporter exclusively, or to several?

If you decide to go ahead, these are things that are okay to say—if you have to: "I'm sorry I don't know the answer to that." "I can't comment on that now." "I would like to clarify that last point." "I'm sorry, I'm unable to help you with that last point."

To a reluctant interviewee, reporters may say: "Your research is supported by public funds; the public has a right to know what you have done with their money." "I am on deadline and will file my story whether you talk to me or not." "I have talked to John Doe, and this is what he has said about the work. Would you like to comment?"

If you want something to be "for background only," or "not for attribution," you must say so at the outset, and secure the reporter's agreement; it does not work retrospectively. Television and radio require concise, quickly understandable responses, which will be less likely to be distorted or taken out of context than a lengthy answer. What you say will always look different in print. Don't use the word "first" unless there is no shadow of doubt that it is so. Be prepared for questions about cost. If you talk about clinical implications, beware of over-interpretation by the reporter, or raising false hopes for the public. If a topic you feel is important does not come up, bring it up; or give it as an answer even if you haven't been asked the question.

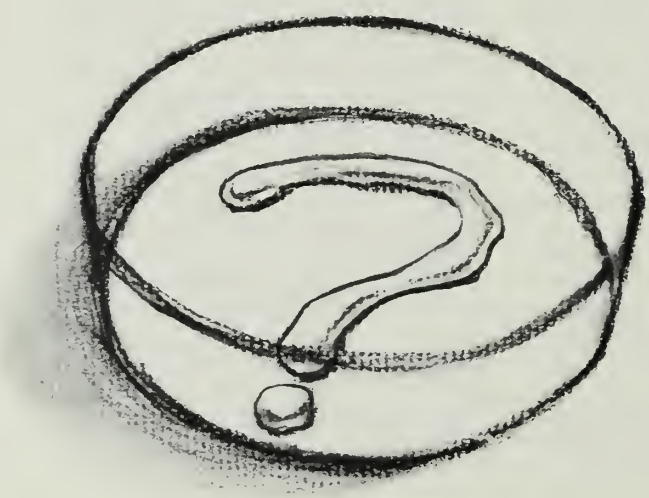
Ask to have your quotations read back to you, or—if it's radio or TV—ask to hear or see a tape before the program is aired. You may not succeed often, but you may improve reporter accuracy in the effort.

—Lillian Blacker

The Making of a Scientist

Students at the Bench

by Lisa Derman



It happens every few years," says pediatric surgeon Judah Folkman '57, perhaps best known for discovering how to prevent tumors from forming new capillaries, without which they are unable to grow. "If you're at the leading edge of a new field, you often don't have a chance to fill in all the details as you go along. Then a student works out a part of the problem that turns out to be absolutely critical."

As a medical student working in Folkman's lab, Michael Gimbrone '69, now associate professor of pathology, developed one of the first techniques to study angiogenesis—the growth of new blood vessels—in the cornea. This study provided compelling evidence that tumor blood vessels are new capillaries arising from the host. David Kessler '77, during his student years in the same lab, found the first clue that the organic acid heparin spurs capillary growth. Stephanie Taylor '84 later extended that finding, which led other investigators in the lab to identify and purify tumor angiogenesis factor. Taylor also experienced one of those rare moments of scientific serendipity: at Folkman's suggestion she added cortisone to her experiments to avoid background inflammation, and found that cortisone and heparin administered together prevent tumor angiogenesis. Only last year, Rosa Crum '85 identified an altered form of cortisone that inhibits angiogenesis without immunosuppressing the animal—an early step toward clinical trials, which still lie far in the future.

The four students profiled below have taken advantage of the many research opportunities HMS offers. As Cedric Priebe '88 did this year, students may on their own arrange with a professor to work in the lab part-time while taking classes—for which they receive no payment. They may spend a summer in the lab full-time, as did James Wong '86—or, as Terri Young '86 did, take a year's leave of absence to pursue investigations. Generally—though Wong and Young are exceptions—the approximately 85 students spending a summer and the dozen or so spending a year in research receive stipends disbursed through the office of Claude Villee, director of the student research program and Andelot Professor of Biological Chemistry.

Those with strong science backgrounds may apply to two established research-oriented programs, the Division of Health Sciences and Technology and the M.D./Ph.D. program. A number, like Bror Saxberg (now in his third year), choose both options—though he is the first ever to enter the two programs simultaneously. In September, the first 25 students to enter the New Pathway Program in General Medical Education (see the Winter 1984 *Bulletin*) will begin the new curriculum, 40 percent of which is reserved for elective work leading to a thesis. That work may take many forms, including basic science investigation.

During the summer after his first year at HMS and part-time during his second year, James Wong helped discover a possible new chemotherapeutic agent.

When I entered HMS, I spent a lot of my study time designing fantastic schemes to help me remember the material presented in lectures," recalls first-year student Cedric Priebe, who worked part-time in Folkman's lab this year on a project he is continuing full-time over the summer. "I decided to apply my creative energy to something more productive and worthwhile. I had been considering a career in medical science, and I wanted to see what it was like to participate in basic science, not just help with routine tasks, as I had done in the summers during college.

"I turned to Judah Folkman. He had given the first and I think the best clinic we've had so far, in which he challenged us always to think of the research side, the unanswered questions."

Nobody knows how many students, like Priebe, participate in research part-time while taking classes, because the arrangements they make are so informal. They receive no payment for their work, and no office asks professors to list the students working in their labs. "We usually take students on a first come, first serve basis," says Folkman, who himself did research part-time during all four years of medical school. "Students come to us as early as September to arrange to do work in our lab the following summer."

Folkman introduced Priebe to Julie Glowacki, assistant professor of surgery, who studies how new bone is formed when demineralized bone powder is injected in mammals. Bone specially processed in her lab has been used in over 200 patients to treat cranial and facial deformities, fractures and cysts in long bones, curvature of the spine, and periodontal disease. In three cases it has also been used to reconstruct children's skulls, removed because they were prematurely fused and could not grow normally as the brain grew.

Priebe is looking at this bone-forming process *in vitro*, trying to grow mouse fibroblast cells on bone powder. "First I have to ask whether the cells have a predilection for attaching to demineralized over regular bone powder," he explains. "I'm amazed at the time I've spent on such a simple thing as counting cells. First I tried to separate the attached from non-attached cells by trypsinizing them. (Trypsin is an enzyme that detaches cells from their substrate.) But that didn't work. So then I tried breaking them up and counting the nuclei. But when I stained them, I found particles of bone powder that looked just like nuclei.

"Everyone in the lab had great ideas about how to solve this problem," he continues, "but the determining factor is to actually carry it through, to work out all the kinks in the method for your system. And that takes a lot of time."

"I've learned that if you want to do medical research, you have to spend a lot of time learning the techniques. I've also learned the importance of teamwork, and not to expect immediate returns."

Outstanding student research is recognized with academic prizes and honors in a special field, both awarded at graduation. In addition, students may present their work at the Soma Weiss Undergraduate Assembly—an annual event, begun by a group of students in 1940 (see sidebar), now held each April after the meeting of the Faculty of Medicine.

This year's assembly included a presentation by third-year student James Wong, who, in the summer

Starting a Tradition

For the past 45 years, Harvard medical students have presented their research to the HMS community at an event now known as the Soma Weiss Undergraduate Assembly—so renamed in 1980, at the request of students, to honor the memory of a faculty supporter of the first Undergraduate Assembly. Below, Gordon Scannell recalls how that first assembly came to be.

The first Undergraduate Assembly of Harvard Medical School was held on April 16, 1940, in Amphitheatre D. It was organized by a group of students who felt HMS undergraduates should have a way of finding out what their classmates were doing by way of investigative work. At the same time, those engaged in research might present their problems and results to an interested audience.

As so often happens, the member of our class (1940) who started the whole thing, Thomas Gephart, gets lost in the shuffle of time. I remember distinctly Tom saying to me, "You know, there's a lot going on around here and some of us conventional clods (he really wasn't) should do something about it. Oh, I know you done in a lot of horseshoe crabs in Arturo ("Muscle-Twitch") Rosenblueth's lab one summer, but the secret of *Limulus polyphemus* is still secret. Let's find out what others are up to."

Tom was a methodical and persistent sort of person. He was later a highly effective secretary of the Massachusetts Medical Society, after a successful career in thoracic surgery. In the fall of 1939 he organized a committee of six from our class: the two of us plus Addison Brenizer Jr., the late John Hickam, Bill Hickey, and Tom Weller; and two from the Class of 1941: Edward Ahrens Jr. and John Schilling.

We agreed the assembly should be primarily an undergraduate affair, but knew instinctively that faculty advice and counsel would be a good thing. We had the utmost cooperation of the students, Dean Burwell, and the faculty, particularly those who consented to serve on the faculty advisory committee: George Minot, Edward Churchill, Baird Hastings, George Wislocki, and Soma Weiss, then in his first year of an all too brief span as chief at the Brigham. Their advice and encouragement were generous and warmly given.

In the 1940 *Aesculapiad* the committee piously went out of its way to point out that the assembly was "in no sense an organization whose aim is primarily to foster student research, but rather an attempt to give expression to a phase of undergraduate activity of obvious importance and interest. It is hoped that the assembly will continue to be an annual affair carried on by the undergraduates under the aegis of a friendly faculty approval and for the interest of undergraduate and graduate alike."

You know, that was a good idea of Tom Gephart's!

Below is a partial list of the papers presented at the first Undergraduate Assembly. Note how naive and understandable are the titles.

Thirty-nine cases of appendicitis in a single family pedigree.
Thomas Perry Jr. '40

Studies on the response of the guinea pig thyroid to thyrotropic hormone.
John E. Vander Laan '40 and Willard P. Vander Laan '42

The influence of ionic strength and pH on Electrophoretic mobility.
Bernard D. Davis '40

The blood vessels of the adrenal gland of the cat.
Lawrence Kilham '40

A roller bottle tissue culture system.
Lawrence C. Kingsland Jr. '40

Enterobiasis (Its incidence and symptomatology in 505 children).
Charles W. Sorenson '40 and T.H. Weller '40

The nature of Charcot-Leyden crystals.
James H. Thompson '40.

—J. Gordon Scannell

after his first year at HMS and part-time during his second year, helped discover a possible new chemotherapeutic agent. No stranger to scientific investigation, Wong was already co-author with his Harvard College roommate Richard Ebright of a paper describing their theory of how cyclic AMP activates genes—the first paper solely by college undergraduates ever published in *Proceedings of the National Academy of Sciences*.

Though he did no research during his first year of medical school ("I had to learn anatomy and physiology, which was very difficult for me; I had never seen anything bigger than a cell when I came here"), Wong was back in the lab the following summer, supported by an American Cancer Society Fellowship.

"I decided if I was going to spend a summer doing research, it should be on something meaningful to me," he says. "I'm interested in cancer, in the applied side." Lan Bo Chen, associate professor of pathology and Wong's tutor at Harvard College, indicated that he had a project that might interest his old student.

Over the past few years, investigators in Chen's lab had learned that a compound called rhodamine 123 is selectively taken up by the mitochondria of tumor cells, and then kills the cells. Since rhodamine 123 is lipophilic (lipid-soluble) and cationic (positively charged), they reasoned, perhaps other compounds with the same characteristics would kill tumor cells more effectively. But first they had to prove that the lipophilic and cationic properties of rhodamine 123 were what caused its uptake.

"The mitochondria make energy for the rest of the cell, as Boston Edison does for Boston," Wong explains. "In order to make energy, they must carry an electrical potential—a difference in charge between inside and outside the mitochondria." Chen hypothesized that the mitochondria of tumor cells are more negatively charged than those of normal cells, and so attract more of the positive-charged rhodamine 123.

Wong worked with post-doctoral fellows Michael Weiss and Samuel Davis to test Chen's hypothesis. They eliminated the mitochondrial potential in both normal and tumor cells, and found practically no uptake of rhodamine 123 (which is fluorescent), or another lipophilic, cationic substance that is radioactive, in either. The small amount of uptake that still occurred in tumor cells was almost

indistinguishable from the amount remaining in normal cells—thus confirming the hypothesis.

After further experiments, the team looked for other compounds that might selectively kill tumor cells. "We tested every lipophilic, cationic compound in the Merck Manual," says Wong. "Now, some might say that's not very scientific. But we weren't just randomly picking compounds from the shelf; we had a hypothesis. Through all that testing, we came up with an agent called dequalinium chloride.

"The selectivity of the chemotherapeutic agents we now use to treat cancer is largely in the ratio of two to one, meaning that if we double the dosage that kills tumor cells, then normal cells will die too," Wong explains. "Dequalinium chloride is taken up by tumor cells in tissue culture from 20 to 1,000 times more than by normal cells, so we could potentially choose a dosage that would kill tumor cells but only minimally affect normal cells."

Would dequalinium chloride work in animal systems? The post-docs and Wong put mouse bladder tumor cells into mice and treated them with dequalinium chloride. The treated mice survived 250 percent longer than the controls (the National Cancer Institute says that prolonging survival by 150 percent is significant). "If you can cure rats, that's nothing if you can't cure humans," says Wong. They grafted human colon cancer cells into nude mice (which are immunodeficient, so they will accept cells from other species), injected dequalinium chloride, and found that it inhibited tumor growth. Would it work on tumors that arise spontaneously in the animal rather than from a cell line grown in tissue culture? They injected rats with a carcinogen in cigarette smoke which causes mammary tumors; again, the treated rats developed fewer tumors than the controls.

"When people come to a hospital with cancer, they already have a tumor big enough to see, so an effective drug must be able to regress tumors, not just arrest them," argues Wong. "We let the rat tumors grow big, and then injected dequalinium chloride. In over 50 percent of the rats, the tumors shrank; some tumors could not be found anymore.

"So one can ask: Is dequalinium chloride the final drug? Is it the cure for cancer?" Wong continues. "I don't think so. By no means. We'll try to screen a lot of agents we haven't tried before, and see if we can come up with others that may be more potent, but dequalinium chloride is a start." Though Wong no longer works in Chen's lab (he is now in clinical rotations), others there are screening thousands of compounds, to try to come up with ever more potent selective chemotherapeutic agents.

Although she had won several fellowships, Terri Young did not plan a clinical research career when she entered HMS, partly, she says, because of a lack of role models.

My interest has always been on the biochemical/molecular/cell biology level," says third-year student Terri Young. "The thinking on the biochemical level is so neat. The molecules and their components are like dancers: each has its own part, and they interact in very specific ways. Once you have it down in your head how they interact, you can build on that, and apply it to other systems."

Young won a Sarnoff Fellowship to do research at Indiana University full-time last year. She also recently won a Commonwealth Fellowship—created by the National Medical Fellowship Program "to encourage mentor relationships between academically gifted minority medical students and noted biomedical scientists"—to pursue more research for two months during the next academic year.

Young first developed an interest in science at Cass Technical High School, a selective public school in Detroit. She spent three summers working in Ford Motor Company's chemistry labs to help pay for her education at Bowdoin College in Maine, and another summer at Battelle Memorial Research Institute. A combined biochemistry-sociology major, she won a Surdna Undergraduate Fellowship her senior year to do an independent research project, using the purified DNA polymerase protein to try to develop a system for replicating the DNA of herpes simplex virus outside the virus itself.

Young did not plan a clinical/research career when she entered HMS, partly, she says, because of a lack of role models. "My college professors and the people I've worked with in labs have all been very encouraging," she says, "but none of them were women or blacks or other minorities. I think there's something to be said for being able to identify with someone—when you say 'I'd love to do what they're doing,' because you see so much of yourself in them, or you'd like to see so much of them in yourself." She found a similar lack of role models during her first two years at HMS, until she met associate professor of medicine Eva Neer, under whom she will do research for her Commonwealth Fellowship next year.

For her Sarnoff Fellowship, Young spent last year in research under Dr. Watanabe, head of medicine and cardiology at Indiana University School of Medicine. "You really can't accomplish anything in two months, or even three or four," she has learned. "You can't do much in a year either, but at least you have plenty of time to get the techniques down." She chose a project she could start up herself, which she says allowed her to "work on it, think about it, be more creative, rather than picking up something someone else had already done."

Young investigated the adenylate cyclase system—a hormonal receptor mechanism in many cells and organ systems which, through a series of interactions, creates cyclic AMP (a messenger molecule) from ATP (the molecule in which the cell stores energy). Her project was to identify the regulatory protein that inhibits this reaction in dog heart cells, following the protocol that had been used to identify the equivalent stimulatory protein.

"I used a probe called islet activating protein (IAP), which is a protein eluted by the Bordetella pertussis organism (the causative agent of whooping cough)," she explains. "The major problem I ran into was purifying the toxin, which wasn't commercially available at the time. It took a week to grow it in huge flasks. Sometimes it grew; sometimes it didn't. Purifying it took another week. When no protein is rendered at the end, it's quite frustrating, because IAP is just a reagent—only one necessary component. We weren't even at the meat of the project."

Finally, Young purified enough toxin to modify the regulatory protein, so she could attach a radioactive

marker to it. She then passed the protein through a gel to find its molecular weight. "We found it!" she exclaims. "We also identified a couple of its properties in dog heart.

"I saw Dr. Watanabe at the American Federation of Clinical Research national meeting in Washington, D.C., recently," Young recalls. "Because of my research, people in his lab are now able to do some of the things we discussed last year. It's neat when you can see that you've provided one building block."

Each year, 25 students from HMS's entering class are admitted to the Health Sciences and Technology program, which is run jointly by MIT and HMS. HST students, chosen for their strong science backgrounds, take their preclinical courses at HMS and MIT separately from their regular HMS classmates, whom they later rejoin for clinical clerkships. HST students are required to turn in a thesis based on laboratory research, clinical investigation, or critical analysis of a significant medical problem; they generally spend three to four months in the lab and then another month or so writing the thesis.

The HST preclinical curriculum examines each organ system separately, teaching its physiology and pathology congruently. "For example, in our cardiovascular pathophysiology, we learn both how the heart and circulatory system functions and how it malfunctions," explains Bror Saxberg, an HST student. "HST courses are more research-oriented than regular HMS courses," he continues. "The classes are small—typically fewer than 30 students—and the professors talk in depth about current research."

Not surprisingly, approximately 50 percent of the HST students apply to the M.D./Ph.D. program during their second year. About half of them—and the same proportion of regular HMS applicants—are accepted into the program. This year 12 out of 23 applicants were accepted, bringing next year's total enrollment up to 73. After completing their preclinical work, M.D./Ph.D. students spend the next two to four years in full-time research in a graduate department, supported by a monthly stipend of approximately $450 from the M.D./Ph.D. program, most of which comes from the NIH Medical Scientist Training Program grant, supplemented by other, private, sources. After completing the dissertation, they begin clinical clerkships.

"We M.D./Ph.D. students are funny beasts," says Bror Saxberg. "It's important for us to hear not just about the clinical side or just about the research side, but how people manage to combine the two."

Saxberg was the first student ever accepted to the HST and M.D./Ph.D. programs simultaneously. Now in his third year, he has completed his required preclinical classwork for HST and his master's thesis for MIT's Department of Electrical Engineering and Computer Science. His thesis topic was an extension of the questions that made him—a mathematics and electrical engineering major at University of Washington who won a Rhodes Scholarship in math—decide to go to medical school in the first place: What are the similarities and differences between computers and the human brain? Can we use computers to study the brain?

"In order to study brain science and computers, it is important to understand a lot about human beings and their biology," Saxberg argues. "Because the parts of a human being are all interconnected, there's a good chance that the molecular or cellular tricks or gizmos used in one part of the body may be used in another way in the brain. I needed an intensive general education in human anatomy, so I knew I needed to go to medical school."

Saxberg's master's project was to determine the minimum information a person or a computer needs, when looking at a ball flying through the air under the influence of gravity, to figure out where the ball came from and where it is going.

"If you were staring at a ball coming at you, that ball as it traveled would in a sense draw a little arc on your retina. Can a person or a computer get enough information from seeing that arc being 'drawn' over time to figure out where the ball is coming from and where it will land?" he asks.

For computers, he found, the answer is yes, but for humans it's more complicated. Saxberg designed a video game in which the object was to "catch" a ball by moving a little triangle on the screen. When the screen showed only the position of the ball as it moved through the air, but gave no other information, people performed poorly. They were much more successful when the ball grew larger as it approached, as it would appear to do in real life.

"My video game showed a negative result: we probably don't use the information contained in the trajectory itself in the way I had suggested could be done in theory," he concludes. He expects to spend the next several years working on a Ph.D. project, which he says will probably be in the area of how motion and perception interact. Then he will begin his clinical clerkships.

"It's fairly stressful for someone who has spent two or three years doing Ph.D. research to suddenly be faced with clinical clerkships," he says. To alleviate this stress, the M.D./Ph.D. program offers a longitudinal clinical course in which students doing research go into the hospital once a week, do a history and a physical exam, present to a doctor, and have their performance evaluated. "It gives them a chance to keep from getting too rusty," explains Saxberg. The program also sponsors a series of lectures and an annual retreat, during which investigators talk about both their research and how they made life decisions such as when to have a family. "We M.D./Ph.D. students are sort of funny beasts," says Saxberg, "so it's important for us to hear, not just about the clinical side or just the research side, but how people manage to combine the two."

What of the future? Cedric Priebe will continue doing research in some field next year. He is considering applying to the M.D./Ph.D. program, and envisions a career combining surgery and research. James Wong expects to begin a fellowship in oncology after he finishes his residency, and then to go on to applied research. Terri Young will also follow a clinical/research path: "From what I've seen here, that doesn't seem too unreasonable to attain," she says. Bror Saxberg, not having experienced clinical clerkships yet, isn't sure whether he wants to concentrate on the research or the clinical side, but knows he will somehow combine the two.

Who knows? Maybe a lecturer will inspire the next generation of HMS undergraduates by telling of these students' findings. □

The Way of Walter B. Cannon

by Marian Cannon Schlesinger

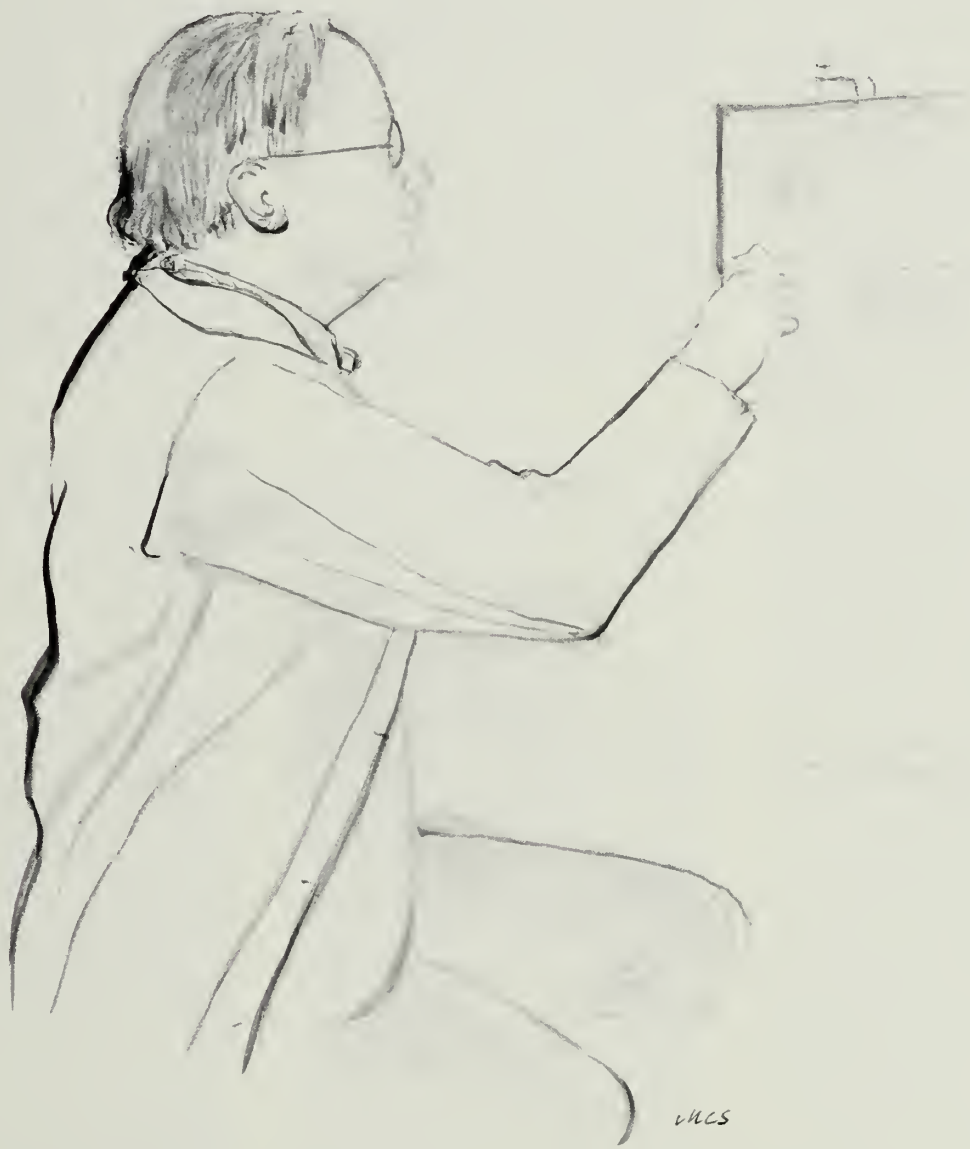


ILLUSTRATION BY MARIAN CANNON SCHLESINGER

First to use X rays to study digestive functions (while still a Harvard medical student), author of the classic Bodily Changes in Pain, Hunger, Fear and Rage *(1919), first to study and articulate the "fight or flight response," and originator of the idea of homeostasis, physiologist Walter B. Cannon was the consummate 20th-century scientist.*

Below, in an adaptation of selections from her memoir Snatched from Oblivion *and a recent talk at a meeting of HMS's Cannon Society, Marian Schlesinger — Cannon's daughter — paints a vivid picture of the scientist outside his laboratory.*

Some time ago, I happened to run into the eminent Harvard psychologist B. F. Skinner at a gathering on Cape Cod and we fell to discussing my father, Walter B. Cannon, who had been for many years professor of physiology at Harvard Medical School, and whose student he had been. My father had been a friend of Ivan Pavlov, the great Russian physiologist, and there was some discussion as to whether there existed any photographs of the two men together. I recalled having seen in the family album a snapshot of the two men taken when Pavlov came to this country for the International Physiological Congress held in Boston in 1919. I promised to go back to Cambridge and look it up.

A few weeks later, I was idly examining some framed photographs on the wall of my sister's house in New Hampshire and saw there an enlarged photograph of Pavlov, my father, and the whole family taken against the hills of New Hampshire so many years ago. I was struck by how Russian it looked. It might have been from an album from Yasnaya Polyana, Tolstoy's country estate, and used as an illustration in the biography of the famous writer. Even a clump of gray birches and the graininess of the print gave it a feeling of authenticity.

Pavlov stood in the middle, his arms linked to those of my father and my ancient grandfather, who might have been an old retainer on the Tolstoy estate with his white, mutton-chop whiskers and quaint air of 19th-century gentility, and who happened to be exactly the same age as Pavlov. My father, who had a wide, round face and an expression of open simplicity and kindliness, seemed close kin to Pavlov himself, who in turn radiated a feeling of gentleness and high intelligence. They both had a fresh, almost childlike, 'born yesterday' air about them that is so often present in men of imaginative genius.

My father was born in Prairie du Chien, Wisconsin, a sleepy little river town on the upper Mississippi. His mother was a schoolteacher and his father, Colbert Hanchett Cannon, a railway employee. It always intrigued my father that it was in this small town of his birth, the site of old Fort Crawford, that in the 1820s the American army surgeon William Beaumont, the 'backwoods physiologist,' as Osler called him, made his classic observations on digestion; some 75 years later my father was in turn to make *his* classic observation of digestion. Using a primitive apparatus of the newly discovered X ray to watch a pearl button pass down the esophagus of a goose, he was able for the first time in history to study the motor activity of the alimentary canal under conditions uncomplicated by anesthesia or operating procedure.

His mother, a highly sensitive, perceptive, and unselfish woman, died tragically when my father was 10 years old, leaving a motherless family of my father and his three younger sisters to be raised by a moody, difficult father. Before she died, my grandmother called the broken-hearted 10-year-old boy to her bedside and said tenderly, "Walter, be good to the world." My father writes: "That wish was most natural for her; it fixed deeply in her son a sacred and haunting memory."

My father was an indifferent student, and his father removed him from school at the age of 14 and put him in the railroad office, where he worked for two years as a timekeeper. This experience at a youthful age seems to have had two effects. For one thing, it made him fanatical about time so that for the rest of his life he was compulsively 'on time,' consulting his watch in an excess of anxiety should he be even moments late. For another, he returned to school and never looked back. He was valedictorian of his high school class—and at the urging of his English teacher, Miss May Newson, he applied for and was admitted to Harvard College, from which he graduated in 1896. Miss Newson had rather a record of sending able students to Harvard. President Eliot had told the admitting office to "accept anyone May Newson recommends." His father gave him his railroad passage and $100. Other than that he worked his way through college with scholarships, tutoring, or waiting on tables at the long-forgotten Fox Gold Club.

Harvard College was a new experience: listening to lectures and having to take notes. My father tells a story about sitting next to a battered football player in one of his first classes and turning to him for advice as to what to put down in his notebook. He growled back *sotto voce*, "Wait till he says something loud. Put that down." His college career, after a slow start, ended successfully, as he graduated summa cum laude and went on to Harvard Medical School, where, when he received his degree in 1900, he was offered an instructorship in physiology. In 1906 he succeeded Henry P. Bowditch as George Higginson Professor of Physiology, an appointment he held until he became professor emeritus in August 1942.

My father demanded proof of himself, and required it of us children. He would bring us down to earth with, "What are the facts?" after some extreme pronouncement.

My father's student years were a period of great intellectual excitement, during which he was attracted by various intellectual disciplines. Among his most influential teachers was William James, whom he found fascinating in the freshness, constant unexpectedness, and phrasing of his ideas. "In my eagerness," my father writes, "to take much of knowledge as my province I was attracted at one time toward philosophy. I recall walking home with Professor James after one of his lectures and at the end of our talk confessing my inclination toward philosophic studies. He turned

on me seriously and remarked, 'Don't do it. You will be filling your belly with east wind.' The remark probably sprang from his quick recognition of my lack of fitness rather than from his disdain of philosophy. What ever the reason for his advice, I followed it."

Like the immigrants from Ireland and Italy, my parents came from the middle west into a long-established, closely knit, family-oriented Cambridge of the turn of the century as virtual aliens. My father was one of the first professors 'from away' to breach the sacred precincts of HMS, long considered the private fiefdom of the Boston medical world.

His appointment, along with a number of other 'outlanders,' was an example of the 'new broom,' 'the breath of fresh air,' with which President Eliot was transforming Harvard from its classical and somewhat parochial tradition into a university of international renown.

My mother and father decided that Cambridge was the place for them, even though it was far removed from HMS, whose new buildings were being erected along Longwood Avenue in Boston. Most of his colleagues on the medical school faculty lived in Brookline or Boston, but my father preferred the long commute, first by streetcar, and then for many decades in his beloved Fords, for which he had an unswerving devotion. Indeed, his life virtually could be measured out in Ford models, from the Model T's to the Model A's to the various specimens of other models, until he died in 1945. I think his devotion to the Ford stemmed from an early admiration for the uncluttered simplicity and ingenuity of the Model T, which appealed to his own native ingenuity. He liked the fact that a piece of haywire or a hairpin could often restore a failing engine. He was forever experimenting as to how far up the steep hill in Franklin, on which our summer house was perched, he could go, "getting a good running start" before he had finally to press the left-hand pedal to the floor. No one who has never driven a Model T Ford will know what I am talking about, but driving one was one of the big thrills of our youth.

My father was the most undemanding of men, almost to a fault. Perhaps the sheer numbers of strong-minded females that made up the household discouraged any impulse to domination or the heavy hand. He would not have known how to go about it anyway, I suspect, and no doubt he was relieved to be off and away to the peace and order of his laboratory, leaving the discipline of us children to my mother.

His carefulness, his intellectual sobriety, the necessity of proof that he scrupulously demanded of himself and required of us children from an early age, had a profound effect on our mental processes. He would bring us down to earth good-naturedly with, "What are the facts?" after some extreme pronouncement. His scorn for sloppy reasoning and hasty, unverified conclusions was a potent force turning us into a tribe of unregenerate rationalists. My mother's mind was almost the exact opposite: speedy, emotional, full of ad hoc opinions and conclusions, and usually directly on target on a myriad of different subjects and problems.

My father had a profound commitment to the pursuit of truth in scientific experimentation (as well as in all other facets of his life); the working out of hypothesis by scrupulous verification under laboratory conditions and under the most exacting standards of proof. For that reason, I presume, although intrigued, he was ambivalent in his attitude to Freud and to psychoanalysis. Yet his basic work on the effects of the emotions on the body, summed up in his classic book *Bodily Changes in Pain, Hunger, Fear and Rage*, on which is based much of the modern theory of psychosomatic medicine, dealt with many of the same phenomena that he passionately believed were subject to the rules of cause and effect to be discovered and proved by scientific method and the human intellect. He would often good-humoredly quote Huxley: "The tragedy of scientific inquiry is the slaying of a beautiful hypothesis by an ugly fact."

He was a constant experimenter throughout his life, inside and outside his laboratory. Early in their marriage my mother wrote, "We are trying vegetarianism this month. Walter wants to see its effects on sleep, activity, metabolism etc. It is strenuous on the cook." In his study of the effects of the emotions on the body he became interested in voodoo death, writing a paper about it in 1942. Although he planned at one time to go to Haiti to look into the phenomenon at first hand, his final illness intervened before he could carry out his project. In his old age he used himself as an experimental animal in an informal inquiry into the problems of aging. He was always interested in how things worked and was ingenious and imaginative in creating his own apparatus for experiments in his laboratory. As a medical student in 1897 he fed bismuth to the aforementioned goose, so that he could watch the progress of the pearl button down its long neck by the means of the newly discovered X ray. The Canada goose was enclosed in a cardboard box with its head and neck protruding through the cover. A long collar made of cardboard firmly fixed to the box further surrounded and immobilized the goose's neck. "Thus," my father wrote, "the goose with the appearance of using the most stylish neckwear presented to the fluorescent screen a very satisfactory extent of the esophagus," and became the first subject in which the peristaltic waves of the stomach were observed. This first bismuth meal was the basis for millions of other bismuth and, later, barium meals downed with loathing by human patients submitting their stomach and intestines to be X-rayed.

"Walter thinks his career is over because he is getting no results from his researches," my mother wrote, "a sure preliminary to another meteoric jump."

My father's career as an experimental physiologist was extremely fruitful throughout the 36 years of his professorship at HMS, with over 400 graduate students and colleagues working and collaborating in the physiological laboratory during that span.

As a student my father had found medical textbooks hard going and sleep-inducing and had observed with some envy the enthusiasm of his

roommate, a student at Harvard Law School, where the case system of study was being used. Recognizing the similarity between medical and legal case histories, as a medical school senior in 1900 he wrote an article suggesting that hospital records should be used to teach medicine. In the years that followed, his suggestion was acted upon and the case system of teaching became an integral feature of medical education.

His early studies of the mechanics of digestion and the gastrointestinal tract led eventually to his studies of the effects of the emotions on the body. As he wrote in his autobiography, *The Way of an Investigator*: "The whole purpose of my effort . . . was to see the peristaltic waves and to learn their effects. . . . Only after some time did I note that the absence of activity was accompanied by signs of perturbation and when serenity was restored the waves promptly reappeared. This observation, a gift for my troubles, led to a long series of studies on the effects of strong emotions on the body." And, "The idea flashed through my mind that [these changes] could be nicely integrated if conceived of as bodily preparations for supreme effort in flight or in fighting. . . . The inhibition of digestive activity by emotional excitement . . . was an interruption of a process which is not essential in a life-or-death emergency and which uses a supply of blood urgently needed elsewhere." On the basis of these experiments, carried on over a period of years, he wrote *Bodily Changes in Pain, Hunger, Fear and Rage*. Over the years a large body of research was carried on in his laboratory on the emergency function of the sympathetic-adrenal mechanism and finally on the eventual chemical mediation of nerve impulses.

In the early '30s, as the result of his conviction that "it is important that science be understood in a democracy," he wrote *The Wisdom of the Body*, a fascinating description of the factors involved in the preservation of the internal equilibrium of the body, which he called 'homeostasis.' The book often reads like a book of wonders as it describes the extraordinarily complex internal world of the human animal and the mechanisms by which the body acts to maintain the balance essential for continuing existence. How, for example, the water, sugar, and salt content of the blood is kept constant; how the body temperature, exposed to great fluctuations from within and without, maintains constancy; how in case of an emergency in many organs, the margin of safety to draw on is often 15 times that necessary for rectification. He describes how the processes of repair and adjustment go on independently of conscious thought, triggered by an incredibly sensitive system of automatic indicators, which set the corrective process in operation.

Like many other creative people, my father had periods of depression, in part resulting from a sense of creative aridity when nothing seemed to be coming out the way he had hoped and his ideas had seemed to dry up. My mother was philosophical in the face of such melancholy, writing, "Walter thinks his career is over because he is getting no results from his researches, a sure preliminary to another meteoric jump." No doubt her buoyant optimism may have been irritating at times to one steeped in gloom, but it was the agent that maintained my father's life on an even keel and kept the household spinning along unperturbed by the periods of his despair.

When my father became a full professor, a sensitive Cambridge lady remarked, "I hope he will now give up those disgusting researches on the stomach."

When one of his experiments became exciting or some new idea formed in his mind that promised a fresh insight, he would often confide it to my mother, who, much to his dismay, would soon have it turned into a fait accompli. As she ruefully remarked about this tendency of hers, "An idea to be tested becomes established fact as soon as it enters my brain."

My father's laboratory was his castle and I think in the 36 years during which he presided over it, I visited it only two or three times and then when I was well into adulthood.

There was a basic simplicity and unworldliness about my father combined with a wry sense of humor about himself. Early in their married life my mother reported, "Walter went to dinner a few days ago with some wealthy Boston doctors. They were talking about what they would do if they had all the money they wanted. Dr. B asked Walter what he would do and he answered, 'I have all the money I want. Mrs. Cannon gives me ten dollars a month and that is enough to buy my lunches, pay my carfare and get my hair cut.' "

When my father's academic title was advanced to full professor, a sensitive Cambridge lady who had learned somehow that he was working on the activities of the digestive tract was heard to remark, "I hope that he will now give up those disgusting researches on the stomach." He observed with some amusement that he was not aware of becoming "more refined" as his interests turned from concern with the alimentary canal to studies on the influence of the emotions on the body.

In the summertime, we all repaired to the family farm in Franklin, New Hampshire, with my father coming up for weekends in July and spending all August there, often writing in his study, a tiny, brown shingled shack like something out of "Hansel and Gretel." It was hidden away at the foot of the towering twin pines that gave our farm its name, built on top of the boulder that was the overhanging backdrop for the woodsy stage where every summer for years we put on plays. He was sometimes forced to evacuate his little aerie when it was used as a Scottish Castle in *The Lady of the Lake*, or a Greek temple in *Alcestis*. But usually the absolute quiet of his retreat was broken only by the sounds of crickets in the hay fields or the croaking of the frogs in the nearby frogpond.

My father was known as "Doc" to the neighboring farmers in New Hampshire, who consulted him not only about their ills but those of their cows and horses. Their faith in him was touching and as Mrs. Patten, the wife of a farmer 'up the hill' who had been ailing all one winter, said, "I told Mason, didn't I, that if I could see Dr. Cannon I would be well."

In the spring of 1929 my father came home from his laboratory one day

and announced that he had just refused an invitation to be visiting professor at the École de Médecine of the University of Paris in the following spring. He saw no reason to uproot himself from his work, interrupt his experiments, disrupt the even tenor of his life to lecture in a foreign language, eat unfamiliar food, and sleep in alien beds. My mother, not one to take such a decision lying down, especially one that involved travel, announced in turn to my father that he should return to his laboratory and immediately withdraw his refusal. "After all, Walter, what an opportunity for the girls." My brother, who seemed to be perpetually being educated, had to stay home and keep his nose to the grindstone, as he was firmly launched in medical school and could, it must be presumed, do without the European 'polishing' reserved for his sisters.

My father went back to his laboratory and withdrew his refusal, though he stood his ground, deciding that half a year was enough for him.

He had last been in France during the First World War as a member of the Harvard Hospital Unit headed by Harvey Cushing, one of the early American medical teams to be sent to the front. There he had worked with British and American colleagues on the problem of shock in the terribly wounded soldiers brought into the base hospitals at Béthune, at Dijon, and at the end of the war at Ecury during the last great German attack in the Châlons-sur-Marne area in 1918.

Many of the observations he and his colleagues made, and that he described in his book *Traumatic Shock*, published in 1923, still hold today even though interpretation of some of the data on shock has changed as time has gone on.

His return to Paris, then, in 1930 was full of memories of an extraordinary time in his life, "the parenthesis of war," as he called it.

International politics permeated the air in the last years of the '30s, and my father's involvement in medical aid to the victims of the Spanish Civil War was a constant theme throughout my mother's letters. Because of his espousal of the Loyalist cause, he was the object of scurrilous attacks not only by local and federal authorities but by conservative members of his own profession, a state of affairs that prompted his friend Professor Ralph Perry to remark to my mother, "the kind of people who excoriate him for his advocacy of Loyalist Spain makes me sure that he is right!" Being a sensitive and idealistic man, he was often deeply depressed when his motives and character were impugned. However, he had fought the good fight for things he believed in throughout his life and did not withdraw from the battle when things got hot or unpleasant. When the Japanese invasion of China exploded, he took up the cudgels again, working for aid to the beleaguered Chinese. He was instrumental in finding jobs in this country for some of his distinguished Jewish physiological colleagues fleeing from Hitler's purges and once wrote a most moving letter describing the extraordinary contributions of the Jews to medicine. It said in part:

My father's espousal of the Spanish Loyalist cause made him the object of attacks not only by authorities, but by conservative members of his own profession.

> The advancing front of medical science owes no debt to narrow patriotism. . . . In the appallingly unjust and cruel measures which Germany and Italy have taken against the Jews, there is utter disregard of the great benefactions to all mankind which have come through Jewish contributions to medical science and art. Is a Hitlerite bleeding to death and desperately dependent on a blood transfusion? His life is saved by methods revealed by Landsteiner, a Jewish Nobel Laureate who showed how to avoid the fatal mixing of incompatible bloods. Does the Italian doctor wish to know whether a patient has typhoid fever? He applied observations first made by Widel, a Jew. Is one of our children in danger of diphtheria? Her resistance to that infection is tested by a process invented by Schick, a Jew—a process which, wisely utilized, could wholly eradicate that once terrifying disease. The tens of thousands of victims of syphilis in countries where antisemitism is rife must rest their hopes for relief on a diagnostic method fundamentally devised by Wasserman, a Jew, and on a curative method discovered by Ehrlich, another Jew chosen as a Nobel Laureate for his beneficent services to mankind. Warburg, Willstatter, Meyerhoff, Friedlander, Schiff, Magnus . . . [and many more] all have advanced medical science and art in such important ways that each is associated with one or more significant contributions. And a host of other Jewish physicians and investigators could be listed who have helped the structure of modern medicine. Throughout medical history the Jewish people have sustained a most illustrious tradition of bringing great gifts to the relief of man's estate. . . . We should all remember that it is the habit of savage mobs to crucify their savior and "know not what they do."

In May 1940, when there was fear that the United States might be drawn into the Second World War, my father was asked to become chairman of a Committee on Shock and Transfusion of the National Research Council, working once again, after a hiatus of 25 years, on the problems of wound shock first studied by him and others in France in World War I.

He was, at this time, the single American who was not only a member of the National Academy of Sciences of the United States, but also of the Royal Society of Great Britain and the Academy of Sciences of the USSR — and in the latter capacity served as liaison with Soviet scientists during the war. But his health was failing, and in October 1945, he finally succumbed after a long battle with leukemia, indubitably the result of his exposure to radiation in his early experiments with the newly discovered X ray some 40 years before.

All his children, except his daughter Wilma, who was in Chungking, China, serving as cultural attaché with the American Embassy, gathered with the rest of the family in the old house in Franklin to 'celebrate' his life, which had ended. 'Celebrate' really was the word, for though we mourned his death, there was a kind of exaltation in recalling the richness of that life and the quality of his person: his humor, his kindliness, his fairness, his fresh imagination that never seemed to dry up, his intellectual rigor, and the uncomplaining courage with which he bore the almost intolerable pain of his last years. □

Snatched From Oblivion: A Cambridge Memoir *by Marian Cannon Schlesinger, originally published by Little, Brown, can be ordered from Gale Hill Books, 109 Irving Street, Cambridge, MA 02138.*

The Travel Program Of

Alumni Flights Abroad

This is a private travel program especially planned for the alumni of Harvard, Yale, Princeton and certain other distinguished universities. Designed for the educated and intelligent traveler, it is specifically planned for the person who might normally prefer to travel independently, visiting distant lands and regions where it is advantageous to travel as a group. The itineraries follow a carefully planned pace which offers a more comprehensive and rewarding manner of travel, and the programs include great civilizations, beautiful scenery and important sights in diverse and interesting portions of the world:

TREASURES OF ANTIQUITY: The treasures of classical antiquity in Greece and Asia Minor and the Aegean Isles, from the actual ruins of Troy and the capital of the Hittites at Hattusas to the great city-states such as Athens and Sparta and to cities conquered by Alexander the Great (16 to 38 days). *VALLEY OF THE NILE:* An unusually careful survey of ancient Egypt that unfolds the art, the history and the achievements of one of the most remarkable civilizations the world has ever known (19 days). *MEDITERRANEAN ODYSSEY:* The sites of antiquity in the western Mediterranean, from Carthage and the Roman cities of North Africa to the surprising ancient Greek ruins on the island of Sicily, together with the island of Malta (23 days).

EXPEDITION TO NEW GUINEA: The primitive stone-age culture of Papua-*New Guinea,* from the spectacular Highlands to the tribes of the Sepik River and the Karawari, as well as the Baining tribes on the island of New Britain (22 days). The *SOUTH PACIFIC:* a magnificent journey through the "down under" world of New Zealand and Australia, including the Southern Alps, the New Zealand Fiords, Tasmania, the Great Barrier Reef, the Australian Outback, and a host of other sights. 28 days, plus optional visits to South Seas islands such as Fiji and Tahiti.

INDIA, CENTRAL ASIA AND THE HIMALAYAS: The romantic world of the Moghul Empire and a far-reaching group of sights, ranging from the Khyber Pass and the Taj Mahal to lavish forts and palaces and the snow-capped Himalayas of Kashmir and Nepal (26 or 31 days). *SOUTH OF BOMBAY:* The unique and different world of south India and Sri Lanka (Ceylon) that offers ancient civilizations and works of art, palaces and celebrated temples, historic cities, and magnificent beaches and lush tropical lagoons and canals (23 or 31 days).

THE ORIENT: The serene beauty of ancient and modern Japan explored in depth, together with the classic sights and civilizations of southeast Asia (30 days). *BEYOND THE JAVA SEA:* A different perspective of Asia, from headhunter villages in the jungle of Borneo and Batak tribal villages in Sumatra to the ancient civilizations of Ceylon and the thousand-year-old temples of central Java (34 days).

EAST AFRICA AND THE SEYCHELLES: A superb program of safaris in the great wilderness areas of Kenya and Tanzania and with the beautiful scenery and unusual birds and vegetation of the islands of the Seychelles (14 to 32 days).

DISCOVERIES IN THE SOUTH: An unusual program that offers cruising among the islands of the Galapagos, the jungle of the Amazon, and astonishing ancient civilizations of the Andes and the southern desert of Peru (12 to 36 days), and *SOUTH AMERICA,* which covers the continent from the ancient sites and Spanish colonial cities of the Andes to Buenos Aires, the spectacular Iguassu Falls, Rio de Janeiro, and the futuristic city of Brasilia (23 days).

In addition to these far-reaching surveys, there is a special program entitled *"EUROPE REVISITED,"* which is designed to offer a new perspective for those who have already visited Europe in the past and who are already familiar with the major cities such as London, Paris and Rome. Included are medieval and Roman sites and the civilizations, cuisine and vineyards of *BURGUNDY AND PROVENCE*; medieval towns and cities, ancient abbeys in the Pyrenees and the astonishing prehistoric cave art of *SOUTHWEST FRANCE;* the heritage of *NORTHERN ITALY,* with Milan, Lake Como, Verona, Mantua, Vicenza, the villas of Palladio, Padua, Bologna, Ravenna and Venice; a survey of the works of Rembrandt, Rubens, Van Dyck, Vermeer, Brueghel and other old masters, together with historic towns and cities in *HOLLAND AND FLANDERS:* and a series of unusual journeys to the heritage of *WALES, SCOTLAND AND ENGLAND.*

Prices range from $2,225 to $5,895. Fully descriptive brochures are available, giving the itineraries in complete detail. For further information, please contact:

Alumni Flights Abroad

Department HMS 24
A.F.A Plaza 425 Cherry Street
Bedford Hills, NY 10507
TOLL FREE 1-800-AFA-8700
N.Y. State (914)241-0111